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# SEARCH REQUEST FORM

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Dwayne C. Jones

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Art Unit:

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## Search Topic:

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claim 1 and 67 with the added terms and

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This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method for the treatment of cancerous cell growth mediated by RAF kinase, comprising administering a compound of Formula I:

A - D - B

(I)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of up to 40 carbon atoms of the formula: -L-(M-L<sup>1</sup>)<sub>q</sub>, where L is a 5 or 6 membered cyclic structure bound directly to D, L<sup>1</sup> comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L<sup>1</sup> contains 0-4 heteroatoms which are members of the group consisting of nitrogen, oxygen or and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 heteroatoms which are members of the group consisting of nitrogen, oxygen or and sulfur,

wherein L<sup>1</sup> is substituted by at least one ~~substituent selected from the group consisting of~~ -SO<sub>2</sub>R<sub>x</sub>, -C(O)R<sub>x</sub> or and -C(NR<sub>y</sub>) R<sub>z</sub>,

R<sub>y</sub> is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing one or more heteroatoms which are N, S, or O selected from N, S and O and optionally halosubstituted, up to ~~per-halo~~ per-halosubstitution,

R<sub>z</sub> is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms which are N, S, or O selected from N, S and O and optionally substituted by halogen, hydroxy or a and carbon based substituents of up to 24 carbon atoms[5] which optionally ~~contain~~ contains one or more heteroatoms which are N, S, or O selected from N, S and O and is

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are optionally substituted by halogen;

$R_x$  is independently chosen from  $R_z$  moieties or is  $R_a$  or  $NR_aR_b$  where  $R_a$  and  $R_b$  are

a) independently

i) hydrogen,

ii) a carbon based moiety of up to 30 carbon atoms optionally containing one or more heteroatoms which are selected from N, S or and O and optionally substituted by halogen, hydroxy or a and carbon based substituent substituents of up to 24 carbon atoms[7] which optionally ~~contain~~ contains one or more heteroatoms which are selected from N, S or and O and is are optionally substituted by halogen, or

iii)  $-OSi(R_f)_3$  where  $R_f$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing one or more heteroatoms which are N, S or O selected from N, S and O and optionally substituted by halogen, hydroxy or a and carbon based substituent substituents of up to 24 carbon atoms[7] which optionally ~~contain~~ contains one or more heteroatoms which are N, S, or O selected from N, S and O and is are optionally substituted by halogen; or

b)  $R_a$  and  $R_b$  together form a 5-7 member heterocyclic structure of 1-3 heteroatoms which are selected from N, S or and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms which are selected from N, S or and O substituted by halogen, hydroxy or a carbon based substituent substituents of up to 24 carbon atoms[7] which optionally ~~contain~~ contains one or more heteroatoms which are N, S, or O selected from N, S and O and is are optionally substituted by halogen; or

c) one of  $R_a$  or  $R_b$  is  $-C(O)-$ , a  $C_1-C_5$  divalent alkylene group or a substituted  $C_1-C_5$  divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the one or more substituents substituent(s) of the substituted  $C_1-C_5$  divalent alkylene group are ~~selected from the group consisting of~~ halogen, hydroxy, or a and carbon based substituent substituents of up to 24 carbon atoms[7] which optionally ~~contain~~ contains one or

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more heteroatoms which are N, S, or O selected from N, S and O and is are optionally substituted by halogen;

where B is substituted, L is substituted or L<sup>1</sup> is additionally substituted, the one or more substituents are ~~selected from the group consisting of~~ halogen, up to per-halosubstitution per-halo, and W<sub>n</sub>, where n is 0-3;

wherein each W is ~~independently selected from the group consisting of~~ -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -C(O)-R<sup>7</sup>, -NO<sub>2</sub>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, -Q-Ar, or a and carbon based moiety moieties of up to 24 carbon atoms[;] optionally containing one or more heteroatoms which are N, S, or O selected from N, S and O and optionally substituted by one or more substituents which are ~~independently selected from the group consisting of~~ -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NO<sub>2</sub>, -NR<sup>7</sup>C(O)R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup> or and halogen up to per-halosubstitution per-halo; with each R<sup>7</sup> ~~independently being selected from~~ H or a carbon based moiety of up to 24 carbon atoms[;] optionally containing one or more heteroatoms which are N, S, or O selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- or and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, and X<sup>a</sup> is halogen; and

Ar is a 5- or 6-member aromatic structure containing 0-2 heteroatoms which are members ~~selected from the group consisting of~~ nitrogen, oxygen or and sulfur, which is optionally substituted by halogen, up to per-halosubstitution, and optionally substituted by Z<sub>n1</sub>, wherein n1 is 0 to 3 and each Z is ~~independently selected from the group consisting of~~ -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -NO<sub>2</sub>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, or and a carbon based moiety of up to 24 carbon atoms[;] optionally containing one or more heteroatoms which are N, S, or O selected from N, S and O and optionally substituted by one or more substituents which are ~~selected from the group consisting of~~ -CN, -CO<sub>2</sub>R<sup>7</sup>, -COR<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NO<sub>2</sub>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, or and -NR<sup>7</sup>C(O)OR<sup>7</sup>, with each R<sup>7</sup> being independently as defined above.

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5-(trifluoromethyl)-2 phenyl urea ~~ureas of Table 3 above;~~

3-(trifluoromethyl) -4 chlorophenyl urea ~~ureas of Table 4 above;~~

3-(trifluoromethyl)-4-bromophenyl urea ~~ureas of Table 5 above; or~~

5-(trifluoromethyl)-4-chloro-2 methoxyphenyl urea ~~ureas of Table 6 above; and~~

~~ureas 101-103 in Table 7 above.~~

67. (Currently Amended) A method for the treatment of a cancerous cell growth mediated by raf kinase in a human or other mammal in need thereof, comprising administering to a human or other mammal in need thereof a compound which is: selected from the group consisting of the one of the following 3-tert butyl phenyl ureas:

adenoma  
myeloid disorder  
Carcinomas of lung, pancreas, thyroid, bladder, colon

*C*  
N-(3-tert-butylphenyl)-N'-(4-(3-(N-methylcarbamoyl)phenoxy)phenyl) urea or and  
N-(3-tert-butylphenyl)-N'-(4-(4-acetylphenoxy)phenyl) urea; or

one of the following the 5-tert-butyl-2-methoxyphenyl ureas:

N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(1,3-dioxoisindolin-5-yloxy)phenyl) urea,  
N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(1-oxoisindolin-5-yloxy)phenyl) urea,  
N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(4-methoxy-3-(N-methylcarbamoyl)phenoxy)phenyl) urea  
or and  
N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(3-(N-methylcarbamoyl)phenoxy)phenyl) urea; or

one of the following the 2-methoxy-5-trifluoromethylphenyl ureas:

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(3-(2-carbamoyl-4-pyridyloxy)phenyl) urea,  
N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

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*N*-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,  
*N*-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,  
*N*-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridylthio)phenyl) urea,

*N*-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(2-chloro-4-(2-(*N*-methylcarbamoyl)(4-pyridyloxy))phenyl) urea or and

*N*-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(3-chloro-4-(2-(*N*-methylcarbamoyl)(4-pyridyloxy))phenyl) urea; or

one of the following the 4-chloro-3-(trifluoromethyl)phenyl ureas:

*N*-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(3-(2-carbamoyl-4-pyridyloxy)phenyl) urea, /  
*N*-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,  
*N*-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea or and  
*N*-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea;

or one of the following the 4-bromo 3-(trifluoromethyl)phenyl ureas:

*N*-(4-bromo-3-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,  
*N*-(4-bromo-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,  
*N*-(4-bromo-3-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridylthio)phenyl) urea,  
*N*-(4-bromo-3-(trifluoromethyl)phenyl)-*N'*-(2-chloro-4-(2-(*N*-methylcarbamoyl)(4-pyridyloxy))phenyl) urea or and  
*N*-(4-bromo-3-(trifluoromethyl)phenyl)-*N'*-(3-chloro-4-(2-(*N*-methylcarbamoyl)(4-pyridyloxy))phenyl) urea; and

or one of the following the 2-methoxy-4-chloro-5-(trifluoromethyl)phenyl ureas:

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*N*-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

*N*-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

*N*-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(2-chloro-4-(2-(*N*-methylcarbamoyl)(4-pyridyloxy))phenyl) urea or and

*N*-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(3-chloro-4-(2-(*N*-methylcarbamoyl)(4-pyridyloxy))phenyl) urea, wherein said compound is administered in a pharmaceutical composition further comprising a pharmaceutically acceptable carrier.

68. (Currently Amended) A method for the treatment of solid cancers in a human comprising administering to a human a compound of Formula I:

A - D - B

(I)

or a pharmaceutically acceptable salt thereof in a pharmaceutical composition further comprising a pharmaceutically acceptable carrier, wherein

D is -NH-C(O)-NH-,

A is ~~a substituted moiety of up to 40 carbon atoms~~ of the formula: -L-(M-L<sup>1</sup>)<sub>q</sub>, where L is a 5 or 6 membered cyclic structure bound directly to D, L<sup>1</sup> comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L<sup>1</sup> contains 0-4 heteroatoms which are members of the group consisting of nitrogen, oxygen or and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 heteroatoms which are members of the group consisting of nitrogen, oxygen or and sulfur,

wherein L<sup>1</sup> is substituted by at least one substituent which is selected from the group

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consisting of  $-SO_2R_x$ ,  $-C(O)R_x$  or  $-C(NR_y)R_z$ ,

$R_y$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing one or more heteroatoms which are N, S or O selected from N, S and O and optionally halosubstituted, up to per-halosubstitution per halo,

$R_z$  is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing one or more heteroatoms which are N, S or O selected from N, S and O and is optionally substituted by halogen, hydroxy or a carbon based substituent substituents of up to 24 carbon atoms[,] which optionally ~~contains~~ contain one or more heteroatoms which are N, S or O selected from N, S and O and is are optionally substituted by halogen;

$R_x$  is independently chosen from  $R_z$  moieties or is  $R_a$  or  $NR_aR_b$  where  $R_a$  and  $R_b$  are

a) independently

i) hydrogen,

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ii) a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms which are selected from N, S or O and optionally substituted by halogen, hydroxy or a and carbon based substituent substituents of up to 24 carbon atoms[;] which optionally contain contains one or more heteroatoms which are N, S or O selected from N, S and O and is are optionally substituted by halogen, or

iii). -OSi(R<sub>f</sub>)<sub>3</sub> where R<sub>f</sub> is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms which are N, S or O selected from N, S and O and optionally substituted by halogen, hydroxy or a and carbon based substituent substituents of up to 24 carbon atoms[;] which optionally contain contains one or more heteroatoms which are N, S or O selected from N, S and O and is are optionally substituted by halogen; or

b) R<sub>a</sub> and R<sub>b</sub> together form a 5-7 member heterocyclic structure of 1-3 heteroatoms which are N, S or O selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms which are N, S or O selected from N, S and O substituted by halogen, hydroxy or a carbon based substituent substituents of up to 24 carbon atoms[;] which optionally contain contains one or more heteroatoms which are N, S or O selected from N, S and O and is are optionally substituted by halogen; or

c) one of R<sub>a</sub> or R<sub>b</sub> is -C(O)-, a C<sub>1</sub>-C<sub>5</sub> divalent alkylene group or a substituted C<sub>1</sub>-C<sub>5</sub> divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C<sub>1</sub>-C<sub>5</sub> divalent alkylene group are selected from the group consisting of halogen, hydroxy, or a and carbon based substituent substituents of up to 24 carbon atoms[;] which optionally contain contains one or more heteroatoms which are N, S or O selected from N, S and O and is are optionally substituted by halogen;

where B is substituted, L is substituted or L<sup>1</sup> is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo or, and W<sub>n</sub> W<sub>n</sub>, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -C(O)-R<sup>7</sup>, -NO<sub>2</sub>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, -Q-Ar, or a and carbon based moiety moieties of up to 24 carbon atoms, optionally containing one or more

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heteroatoms which are N, S or O ~~selected from N, S and O~~ and optionally substituted by one or more substituents which are independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NO<sub>2</sub>, -NR<sup>7</sup>C(O)R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup> or and halogen up to per-halosubstitution per-halo; with each R<sup>7</sup> independently selected from H or a carbon based moiety of up to 24 carbon atoms[5] optionally containing heteroatoms which are N, S or O ~~selected from N, S and O~~ and optionally substituted by halogen,

wherein Q is -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>- CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- or and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, and X<sup>a</sup> is halogen; and

Ar is a 5- or 6-member aromatic structure containing 0-2 heteroatoms which are members selected from the group consisting of nitrogen, oxygen or and sulfur, which is optionally substituted by halogen, up to per-halosubstitution per-halo, and optionally substituted by Zn<sub>1</sub>, wherein n1 is 0 to 3 and each Z is independently ~~selected from the group consisting of~~ -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -NO<sub>2</sub>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, or and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms which are N, S or O ~~selected from N, S and O~~ and optionally substituted by one or more substituents which are selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -COR<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NO<sub>2</sub>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, or and -NR<sup>7</sup>C(O)OR<sup>7</sup>, with R<sup>7</sup> as defined above.

69. (Currently amended) A method for the treatment of carcinomas, myleoid disorders or adenomas in a human comprising administering to a human a compound of Formula I:

A - D - B

(I)

or a pharmaceutically acceptable salt thereof in a pharmaceutical composition further comprising a pharmaceutically acceptable carrier, wherein

D is -NH-C(O)-NH-,

A is ~~a substituted moiety of up to 40 carbon atoms~~ of the formula: -L-(M-L<sup>1</sup>)<sub>q</sub>, where L

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# STIC Search Report

## Biotech-Chem Library

STIC Database Tracking Number: 116243

TO: Dwayne C Jones  
Location: REM-4C70  
Art Unit: 1614  
Tuesday, March 09, 2004

Case Serial Number: 10/042226

From: Barb O'Bryen  
Location: Biotech-Chem Library  
Remsen E01A69  
Phone: 571-272-2518

barbara.obryen@uspto.gov

### Search Notes

Q is defined but NOT tested Rule 126 claim 44?  
1-3 cancelled  
6,7-13 45, 14, 16, 20  
15, 17-19 22-26, 29-31  
21, 27, 28, 32 34-36, 40-42  
37, 37-39, 43 51, 55-55  
45-50, 52-51  
66-121  
In vitro ref Kinase Assay (p 94)  
human tumor cell lines (p. 95)  
→ HCT116  
OLD-1  
In vivo assay (p. 8)  
→ mice injected w/ human  
colon adenocarcinoma cell line  
Pending applications  
US 09/889,227 -  
US 09/948,915 - 2002/0042517  
US 09/779,920 - 2002/165294  
10/042,203 - paper  
US 09/907,970 - 2002/013774 MW  
US 09/993,647 - 2003/0181442  
10/071,248 - 2  
US 09/771,920 - 2002/165394  
US 2003/207914  
US 2003/181442  
US 2003/144278 (12 JAN 04)  
US 14 of 28 WO/2004/085857  
US 2002/165,394 (07 FEB 2004)  
US 2003/139,605  
2002/165394  
2002/137774  
(12 JAN 04)  
RN No. 15478-166  
\* 21 of 28 RN No. 15478-166  
22 of 28 (SURAMIN)  
23 of 28  
2001/011155  
WO 2000/042012  
8 of 16  
6 of 16  
20 of 28



09/083,399  $\Rightarrow$  6,187,799

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## **DETAILED ACTION**

### ***Status of Claims***

1. Claims 1-3, 6-13, 15, 17-19, 21, 27, 28, 32, 33, 37-39, 4350, 52-54, and 66-121 are pending.
2. Claims 1-3, 6-13, 15, 17-19, 21, 27, 28, 32, 33, 37-39, 4350, 52-54, and 66-121 are rejected.

### ***Information Disclosure Statement***

3. The information disclosure statement filed on September 22, 2003 has been reviewed and considered, see enclosed copy of PTO FORM 1449.

### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims ???? are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.
6. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089, 118 S.Ct. 1548 (1980), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plan for obtaining the

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# STIC SEARCH RESULTS FEEDBACK FORM

## Biotech-Chem Library

Questions about the scope or the results of the search? Contact *the searcher* or contact:

Mary Hale, Information Branch Supervisor  
Remsen Bldg. 01 D86  
571-272-2507

## Voluntary Results Feedback Form

➤ I am an examiner in Workgroup:  Example: 1610

➤ Relevant prior art **found**, search results used as follows:

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☒ Helped examiner better understand the invention.
- ☒ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature  
(journal articles, conference proceedings, new product announcements etc.)

➤ Relevant prior art **not found**:

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC-Biotech-Chem Library, Remsen Bldg.



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=> fil reg; d ide l15

FILE 'REGISTRY' ENTERED AT 15:51:25 ON 09 MAR 2004

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STRUCTURE FILE UPDATES: 8 MAR 2004 HIGHEST RN 660388-34-1

DICTIONARY FILE UPDATES: 8 MAR 2004 HIGHEST RN 660388-34-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

L15 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 139691-76-2 REGISTRY

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

OTHER NAMES:

CN C-raf kinase

CN c-Raf serine/threonine kinase

CN c-raf-1 kinase

CN C-Raf-1 protein kinase

CN c-Raf-1 serine/threonine protein kinase

CN Gene c-Raf protein kinase

CN Gene c-raf-1 phosphoproteins

CN Gene raf serine/threonine kinase

CN Gene raf-1 kinase

CN Gene raf-1 protein kinase

CN p74raf-1 kinase

CN Phosphoproteins, gene RAF-1

CN Protein kinase c-Mil

CN Protein kinase c-Raf

CN Protein kinase Raf-1

CN **Raf kinase**

CN Raf mitogen-activated protein kinase kinase kinase

CN Raf-1 kinase

CN Raf-1 protein

CN Raf-1 protein kinase

CN Raf-1 protein serine kinase

CN Raf-1 protein serine/threonine kinase

CN RAF-1 serine/threonine kinase

CN Raf-1 serine/threonine protein kinase

CN Serine-threonine kinase RAF-1

CN Serine/threonine kinase pRaf-1

DR 144378-33-6

MF Unspecified

CI MAN

SR CA

LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, CEN, CIN, PROMT, TOXCENTER, USPAT2, USPATFULL

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

1799 REFERENCES IN FILE CA (1907 TO DATE)

16 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1802 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil reg; d stat que 194; fil capl; d que nos 199; fil medl cancer; d que nos 1103; d que nos 1112; d que nos 1115; s 1103 or 1112 or 1115  
FILE 'REGISTRY' ENTERED AT 16:59:17 ON 09 MAR 2004  
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

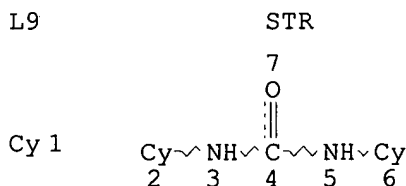
STRUCTURE FILE UPDATES: 8 MAR 2004 HIGHEST RN 660388-34-1  
DICTIONARY FILE UPDATES: 8 MAR 2004 HIGHEST RN 660388-34-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>



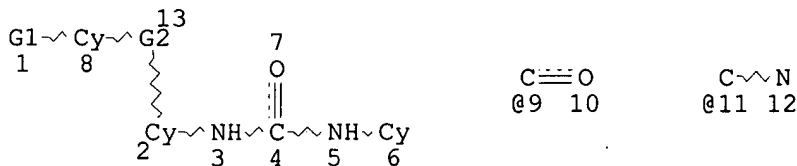
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on this structure*

NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 7

STEREO ATTRIBUTES: NONE

L11 7207318 SEA FILE=REGISTRY ABB=ON NR>2 AND N>1 AND O/ELS  
L13 40386 SEA FILE=REGISTRY SUB=L11 SSS FUL L9  
L91 STR



*subset search done  
on this structure  
(claim 1)*

VAR G1=SO2/9/11  
REP G2=(0-20) A - A = any non-hydrogen atom  
NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE

L94 7087 SEA FILE=REGISTRY SUB=L13 SSS FUL L91

100.0% PROCESSED 40135 ITERATIONS

7087 ANSWERS

SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 16:59:17 ON 09 MAR 2004

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FILE COVERS 1907 - 9 Mar 2004 VOL 140 ISS 11

FILE LAST UPDATED: 8 Mar 2004 (20040308/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L9 STR  
L11 7207318 SEA FILE=REGISTRY ABB=ON NR>2 AND N>1 AND O/ELS  
L13 40386 SEA FILE=REGISTRY SUB=L11 SSS FUL L9  
L15 1 SEA FILE=REGISTRY ABB=ON "RAF KINASE"/CN  
L16 1802 SEA FILE=CAPLUS ABB=ON L15  
L17 268 SEA FILE=CAPLUS ABB=ON L16(L) (INHIB?/OBI OR BLOCK?/OBI OR  
ANTAG?/OBI)  
L19 171014 SEA FILE=CAPLUS ABB=ON ANTITUMOR AGENTS+OLD/CT  
L20 299255 SEA FILE=CAPLUS ABB=ON NEOPLASM#/CW  
L21 13856 SEA FILE=CAPLUS ABB=ON ?ADENOMA?/BI  
L23 130642 SEA FILE=CAPLUS ABB=ON ?CARCINOMA?/BI  
L24 18537 SEA FILE=CAPLUS ABB=ON MYELOID/BI  
L91 STR  
L94 7087 SEA FILE=REGISTRY SUB=L13 SSS FUL L91  
L95 3772 SEA FILE=CAPLUS ABB=ON L94  
L97 62875 SEA FILE=CAPLUS ABB=ON LEUKEMI?/OBI  
L99 19 SEA FILE=CAPLUS ABB=ON L95 AND (L19 OR L20 OR L21 OR L23 OR  
L24 OR L97) AND L17

FILE 'MEDLINE' ENTERED AT 16:59:17 ON 09 MAR 2004

FILE 'CANCERLIT' ENTERED AT 16:59:17 ON 09 MAR 2004

L9 STR

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L13 40386 SEA FILE=REGISTRY SUB=L11 SSS FUL L9  
L43 2700 SEA SURAMIN/CT  
L45 305522 SEA C4./CT(L) DT/CT = Drug therapy of *re* Neoplasms  
L46 186117 SEA L45/MAJ  
L91 STR  
L94 7087 SEA FILE=REGISTRY SUB=L13 SSS FUL L91  
L100 7 SEA FILE=REGISTRY ABB=ON L94 AND (MEDLINE OR CANCERLIT)/LC  
L101 2995 SEA L100  
L103 4 SEA L46 AND L101 NOT L43

L43 2700 SEA SURAMIN/CT - Many, many hits on this compound, so I  
L105 90864 SEA LEUKEMIA, MYELOID+NT/CT gave you only review  
L106 98035 SEA ADENOMA+NT/CT articles  
L107 505305 SEA CARCINOMA+NT/CT  
L108 81568 SEA (L105 OR L106 OR L107) (L) DT/CT  
L109 48256 SEA L108/MAJ  
L110 1238 SEA L43/MAJ  
L112 2 SEA L110 AND L109 AND AB/FA AND GENERAL REVIEW/DT

L43 2700 SEA SURAMIN/CT  
L105 90864 SEA LEUKEMIA, MYELOID+NT/CT  
L106 98035 SEA ADENOMA+NT/CT  
L107 505305 SEA CARCINOMA+NT/CT  
L108 81568 SEA (L105 OR L106 OR L107) (L) DT/CT  
L109 48256 SEA L108/MAJ  
L110 1238 SEA L43/MAJ  
L111 45 SEA L110 AND L109  
L114 1291872 SEA LUNG OR PANCREA? OR THYROID OR BLADDER OR COLON? OR  
COLORECT?  
L115 13 SEA L111 AND L114 - Suramin "NOT" - ed out of this answer set

L121 17 L103 OR L112 OR L115

=> dup rem 199,1121

FILE 'CAPLUS' ENTERED AT 16:59:25 ON 09 MAR 2004  
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FILE 'MEDLINE' ENTERED AT 16:59:25 ON 09 MAR 2004

FILE 'CANCERLIT' ENTERED AT 16:59:25 ON 09 MAR 2004  
PROCESSING COMPLETED FOR L99  
PROCESSING COMPLETED FOR L121

L122 28 DUP REM L99 L121 (8 DUPLICATES REMOVED)  
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ANSWERS '20-28' FROM FILE MEDLINE

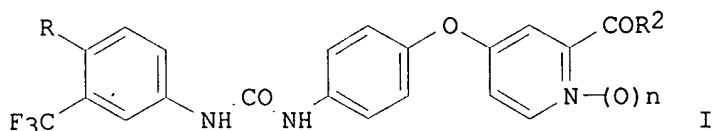
=> d ibib ed abs hitstr 1-19; d iall 20-28

L122 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2003:656745 CAPLUS  
DOCUMENT NUMBER: 139:197377  
TITLE: Preparation of aryl ureas for therapeutic use as  
kinase inhibitors  
INVENTOR(S): Dumas, Jacques; Scott, William J.; Chien, Du-Schieng;

Lee, Wendy; Bjorge, Susan; Musza, Laszlo L.; Nassar, Ala; Riedl, Bernd  
PATENT ASSIGNEE(S): Bayer Corporation, USA  
SOURCE: PCT Int. Appl., 64 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068746	A1	20030821	WO 2003-US4109	20030211
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

US 2003216446 A1 20031120 US 2003-361859 20030211  
PRIORITY APPLN. INFO.: US 2002-354937P P 20020211  
OTHER SOURCE(S): MARPAT 139:197377  
ED Entered STN: 22 Aug 2003  
GI



AB Aryl ureas, such as I [R = Cl, Br; R<sub>2</sub> = OH, NH<sub>2</sub>, NHMe, NHCH<sub>2</sub>OH, alkoxy; n = 0, 1], were prepd. for use in pharmaceutical compns. for the treatment of raf kinase and p38 kinase mediated diseases. These ureas are useful for the treatment of inflammation, osteoporosis, angiogenesis disorders and hyper-proliferative disorders, such as cancer. Thus, urea I (R = Cl, R<sub>2</sub> = NHMe, n = 1) was prepd. with 57% yield by N-oxidn. of I (R = Cl, R<sub>2</sub> = NHMe, n = 0) using 3-chloroperbenzoic acid in CH<sub>2</sub>Cl<sub>2</sub> and THF. The prepd. ureas were assayed for inhibition of p38 kinase and raf kinase, as well as for cancer cell growth inhibition in human cancer cell lines, such as HCT116 and DLD-1.

IT 139691-76-2, Raf Kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(prepn. of aryl ureas for therapeutic use as kinase inhibitors)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

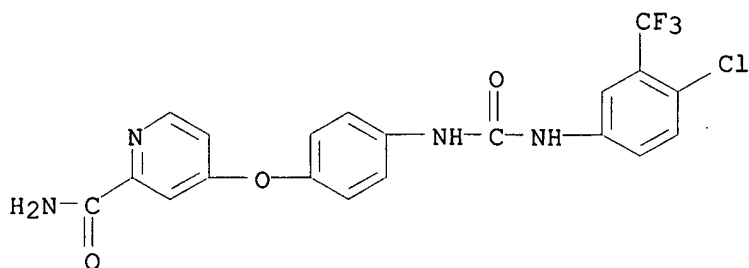
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-carbamoyl(4-pyridyloxy)phenyl]urea 284462-18-6P  
583840-03-3P 583840-04-4P 583840-09-9P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses).  
(prepn. of aryl ureas for therapeutic use as kinase inhibitors)

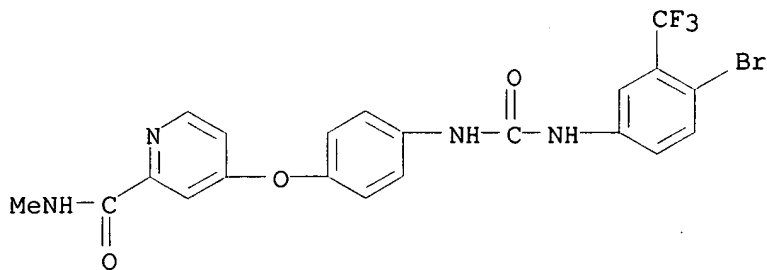
RN 284461-74-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



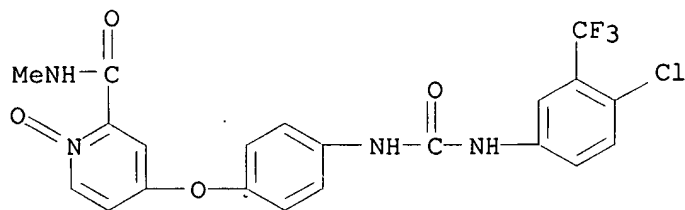
RN 284462-18-6 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



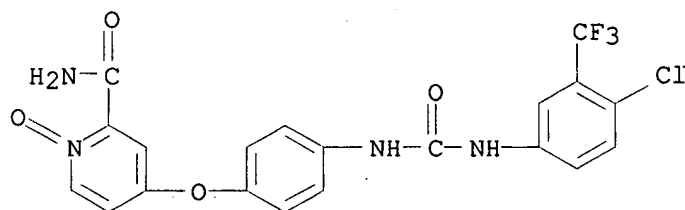
RN 583840-03-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-, 1-oxide (9CI) (CA INDEX NAME)



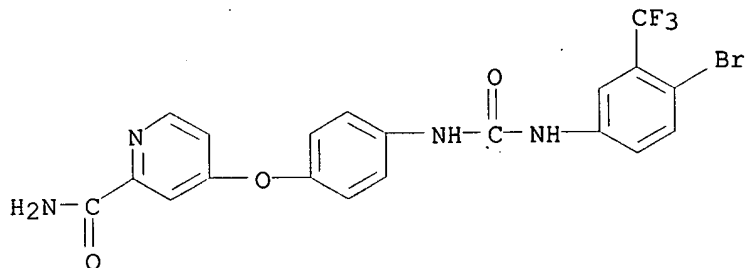
RN 583840-04-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, 1-oxide (9CI) (CA INDEX NAME)



RN 583840-09-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



IT 583840-05-5P 583840-06-6P 583840-07-7P

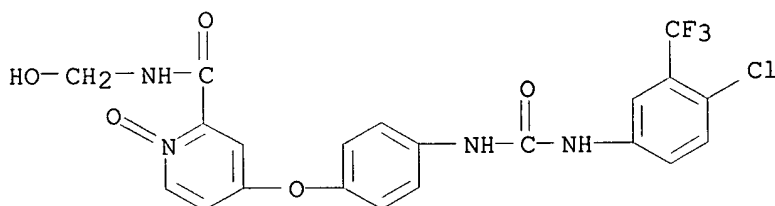
583840-08-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of aryl ureas for therapeutic use as kinase inhibitors)

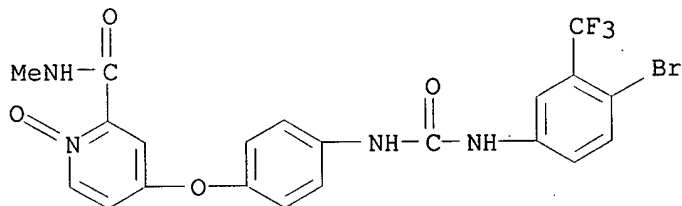
RN 583840-05-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(hydroxymethyl)-, 1-oxide (9CI) (CA INDEX NAME)



RN 583840-06-6 CAPLUS

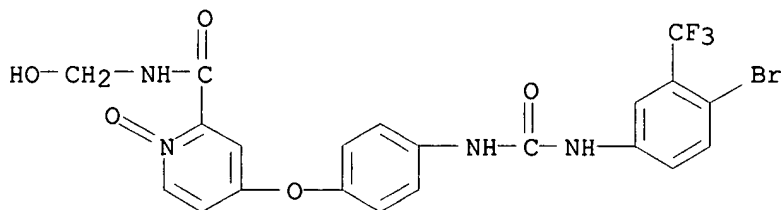
CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-, 1-oxide (9CI) (CA INDEX NAME)



RN 583840-07-7 CAPLUS

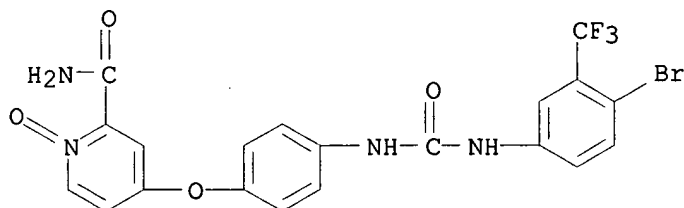
CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(hydroxymethyl)-, 1-oxide (9CI) (CA INDEX NAME)





RN 583840-08-8 CAPLUS

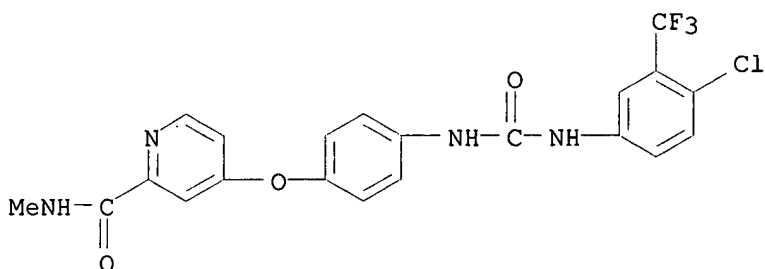
CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, 1-oxide (9CI) (CA INDEX NAME)



IT **284461-73-0P**, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)(4-pyridyloxy)phenyl]urea  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of aryl ureas for therapeutic use as kinase inhibitors)

RN 284461-73-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L122 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:656581 CAPLUS

DOCUMENT NUMBER: 139:197370

TITLE: Preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors

INVENTOR(S): Dumas, Jacques; Scott, William J.; Riedl, Bernd

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 67 pp.

CODEN: PIXXD2

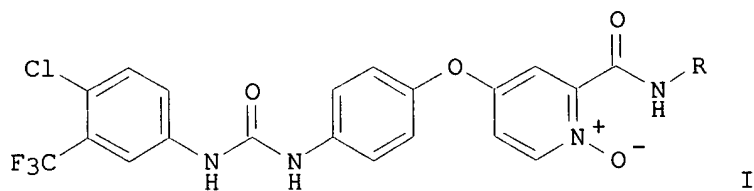
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068229	A1	20030821	WO 2003-US4110	20030211
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003216396	A1	20031120	US 2003-361850	20030211
PRIORITY APPLN. INFO.:		US 2002-354935P P 20020211		
OTHER SOURCE(S):		MARPAT 139:197370		
ED Entered STN: 22 Aug 2003				
GI				



AB The title ureas contg. a pyridine, quinoline, or isoquinoline functionality which is oxidized at the nitrogen heteroatom MLBNHCONHA [A = (un)substituted Ph, naphthyl, 5-6 membered monocyclic heteroaryl, 8-10 membered bicyclic heteroaryl; B = (un)substituted phenylene, naphthylene, 5-6 membered monocyclic heteroarylene, 8-10 membered bicyclic heteroarylene; L = (CH<sub>2</sub>)<sub>m</sub>O(CH<sub>2</sub>)<sub>l</sub>, (CH<sub>2</sub>)<sub>m</sub>(CH<sub>2</sub>)<sub>l</sub>, (CH<sub>2</sub>)<sub>m</sub>CO(CH<sub>2</sub>)<sub>l</sub>, etc.; m, l = 0-4; M = (un)substituted pyridine-1-oxide, quinoline-1-oxide, isoquinoline-1-oxide; with the provisos] which are useful in the treatment of (i) raf mediated diseases, for example, cancer, (ii) p38 mediated diseases such as inflammation and osteoporosis, and (iii) VEGF mediated diseases such as angiogenesis disorders, were claimed. Prepn. of two ureas such as I [R = H, Me] which are not compds. of the invention, and have been distinguished from the compds. of the invention by a proviso, was described. Pharmaceutical compn. comprising the title ureas was claimed.

IT 139691-76-2, Raf kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(prepn. of aryl ureas contg. pyridine, quinoline and isoquinoline  
N-oxide functionality as kinase inhibitors)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

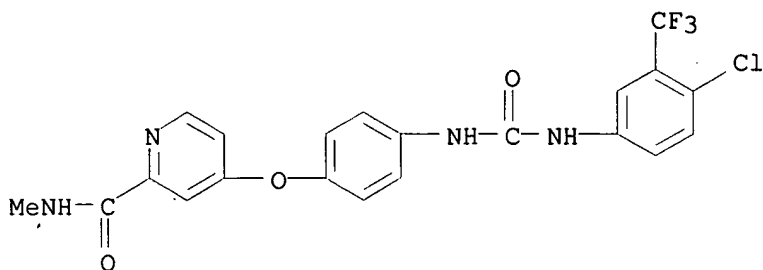
IT 284461-73-0

RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of aryl ureas contg. pyridine, quinoline and isoquinoline  
N-oxide functionality as kinase inhibitors)

RN 284461-73-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c

arbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



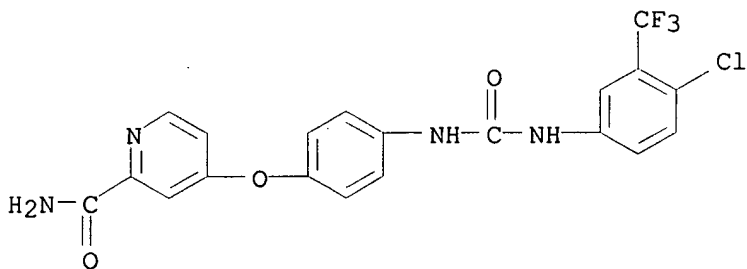
IT 284461-74-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of aryl ureas contg. pyridine, quinoline and isoquinoline  
N-oxide functionality as kinase inhibitors)

RN 284461-74-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



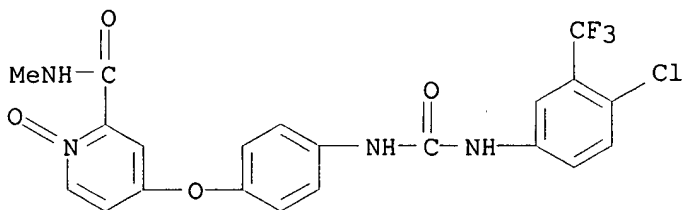
IT 583840-03-3P 583840-04-4P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of aryl ureas contg. pyridine, quinoline and isoquinoline  
N-oxide functionality as kinase inhibitors)

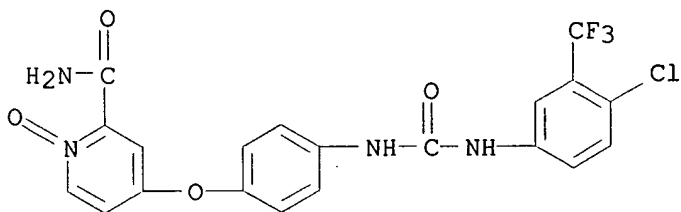
RN 583840-03-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-, 1-oxide (9CI) (CA INDEX NAME)



RN 583840-04-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, 1-oxide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L122 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:656575 CAPLUS

DOCUMENT NUMBER: 139:197476

TITLE: Preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity

INVENTOR(S): Dumas, Jacques; Scott, William J.; Elting, James; Hatoum-Makdad, Holia

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 142 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068223	A1	20030821	WO 2003-US4102	20030211
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

US 2004023961 A1 20040205

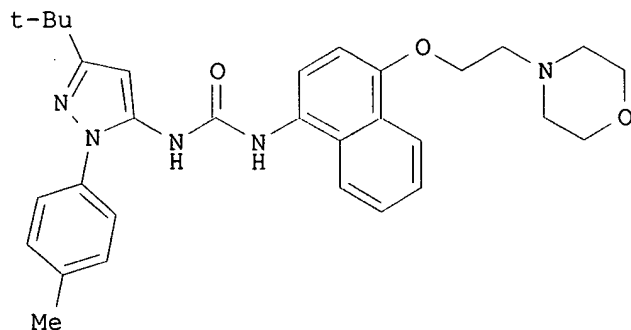
US 2003-361844 20030211

PRIORITY APPLN. INFO.:

US 2002-354948P P 20020211

ED Entered STN: 22 Aug 2003

GI



I

AB 283 Of the title ureas useful for treating diseases mediated by raf kinase and diseases mediated by the VEGF induced signal transduction pathway characterized by abnormal angiogenesis or hyperpermeability processes, were claimed. Synthesis of 6 ureas such as I was described. Thus, reacting 3-(tert-butyl)-1-(4-methylphenyl)pyrazole-5-ylamine with 4-(2-morpholin-4-ylethoxy)naphthylamine (prepn. given) and CDI in CH<sub>2</sub>Cl<sub>2</sub> afforded 80% I which showed IC<sub>50</sub> of < 1 .mu.M in in vitro raf kinase and in in vitro Flk-1 ELISA assay.

IT 139691-76-2, Raf kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(prepn. of aryl heterocyclyl ureas with raf kinase and angiogenesis  
inhibiting activity)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 285984-00-1P 285984-02-3P 285984-03-4P

294848-67-2P 294848-76-3P 294848-91-2P

294848-98-9P 294849-24-4P 294849-28-8P

294849-30-2P 294849-62-0P 294850-35-4P

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294851-48-2P 294851-50-6P 294851-58-4P

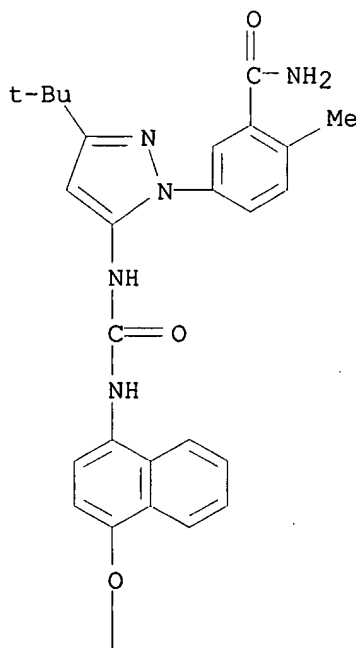
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(prepn. of aryl heterocyclyl ureas with raf kinase and angiogenesis  
inhibiting activity)

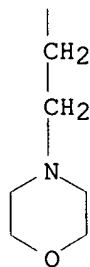
RN 285984-00-1 CAPLUS

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PAGE 1-A

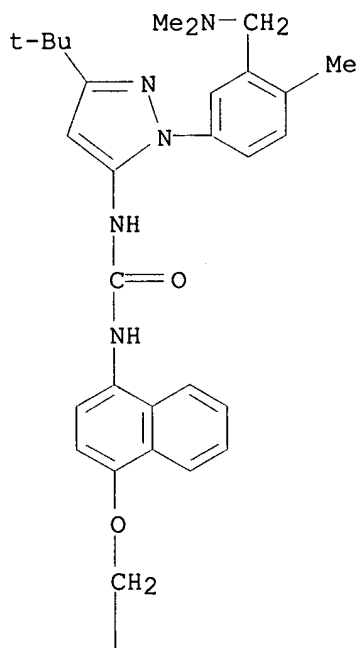


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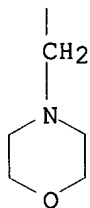


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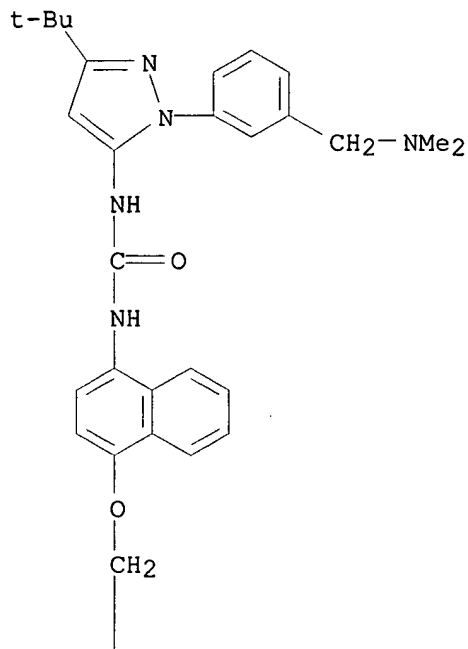
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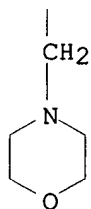
RN 285984-03-4 CAPLUS

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PAGE 1-A

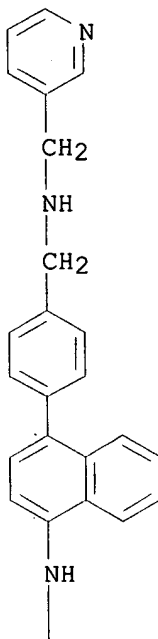


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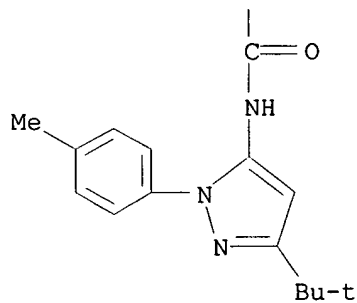


RN 294848-67-2 CAPLUS  
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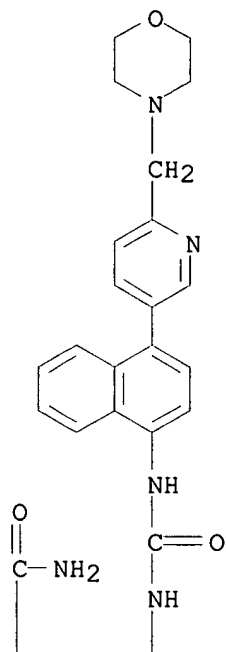
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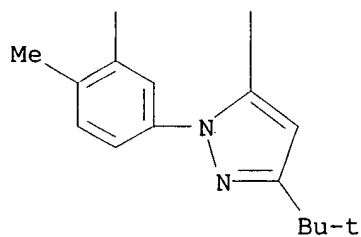
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(9CI) (CA INDEX NAME)



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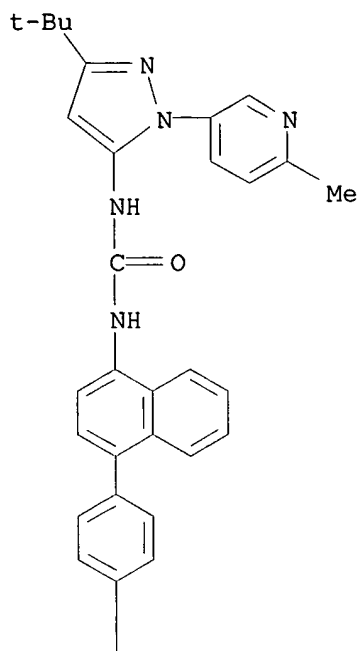


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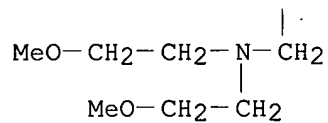


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 (CA INDEX NAME)

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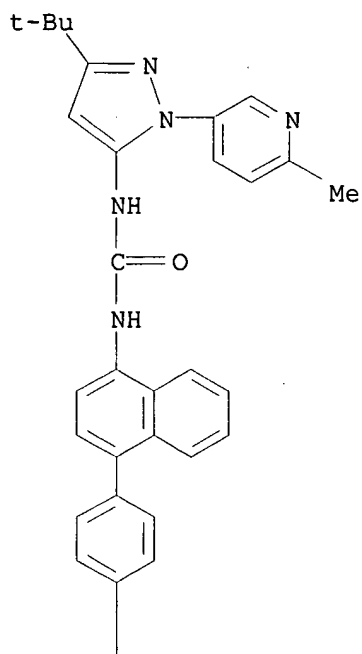


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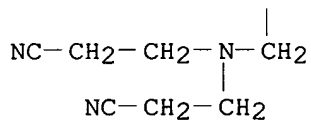


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 (CA INDEX NAME)

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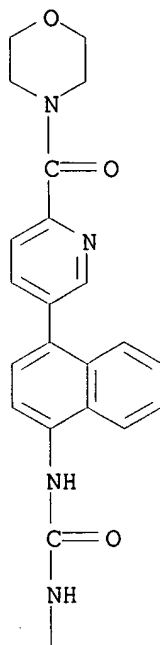


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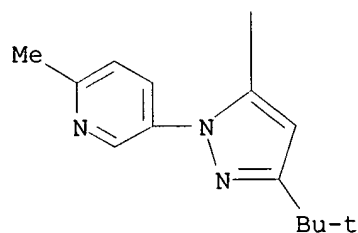


RN 294849-24-4 CAPLUS  
 CN Morpholine, 4-[[5-[4-[[[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]-2-pyridinyl]carbonyl]-(9CI) (CA INDEX NAME)

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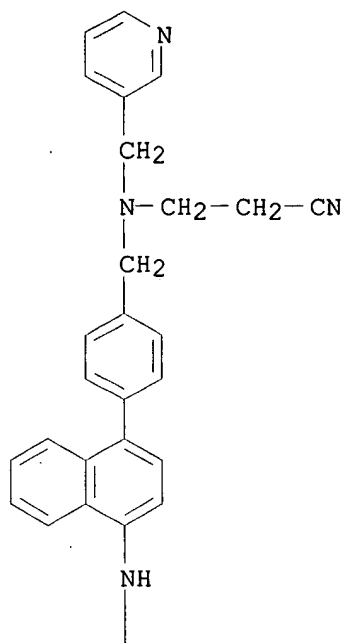


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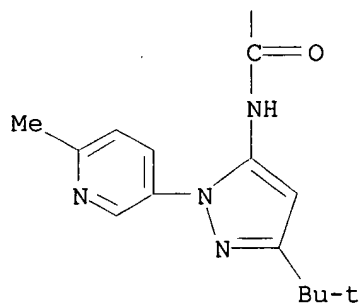


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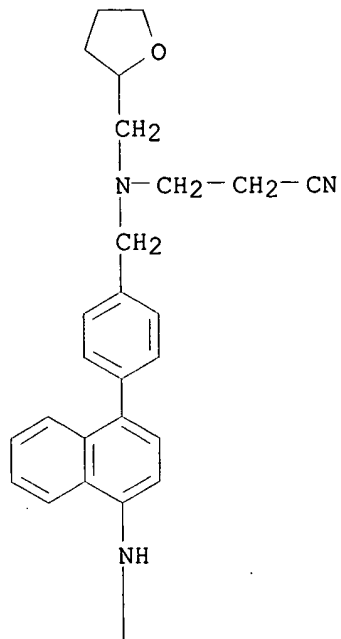


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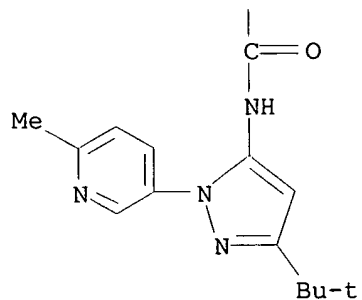


RN 294849-30-2 CAPLUS  
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PAGE 1-A

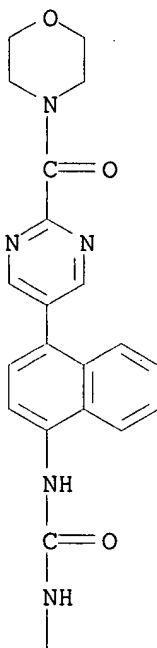


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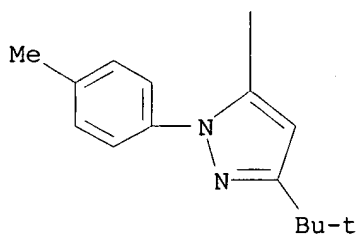


RN 294849-62-0 CAPLUS  
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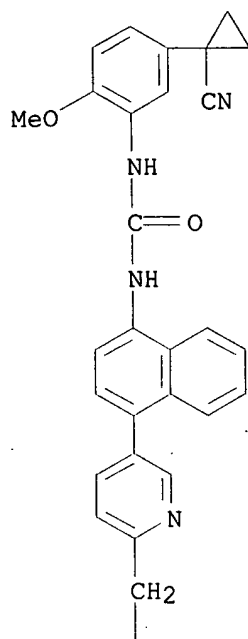


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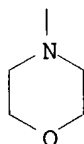


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PAGE 1-A



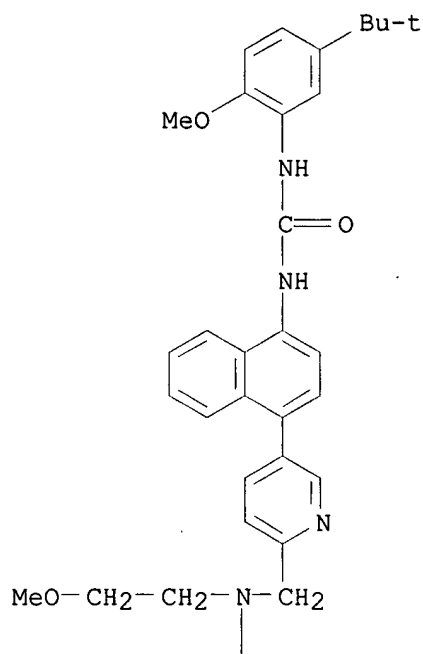
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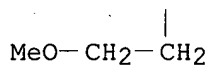
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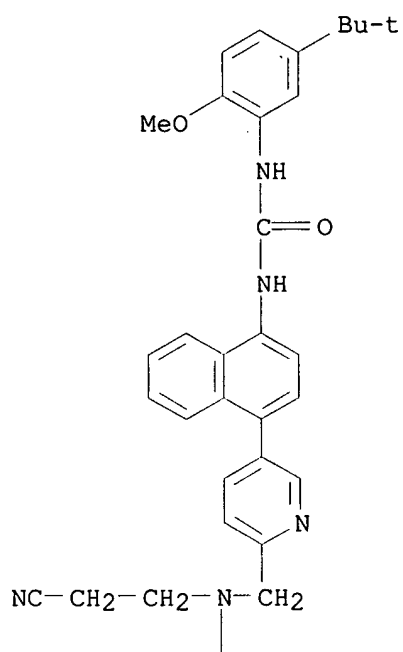


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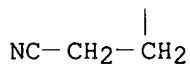


RN 294851-22-2 CAPLUS  
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PAGE 1-A

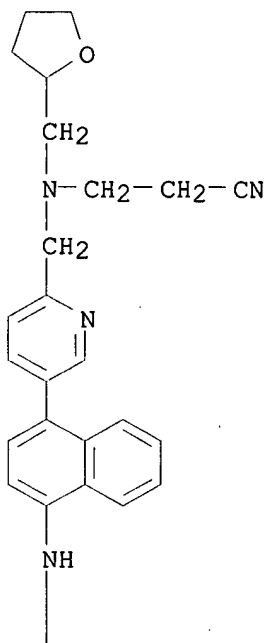


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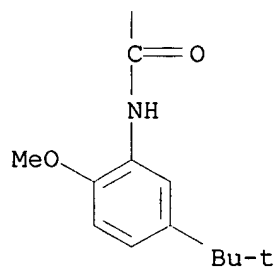


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 (9CI) (CA INDEX NAME)

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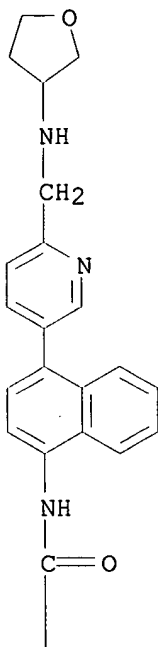


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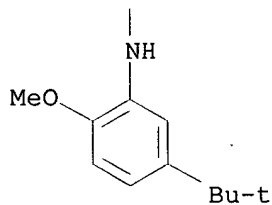


RN 294851-48-2 CAPLUS  
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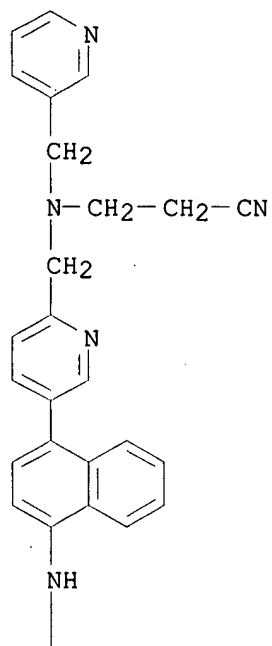


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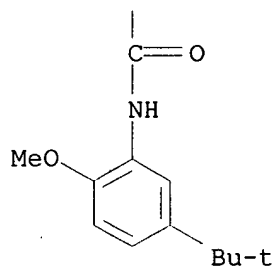


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PAGE 1-A

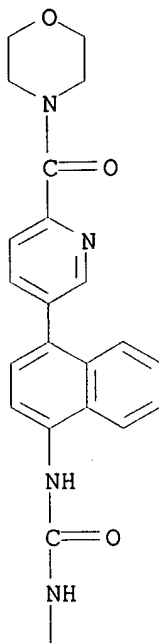


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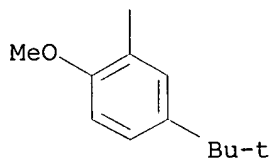


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REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L122 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:633416 CAPLUS

DOCUMENT NUMBER: 139:173786

TITLE: Method for treating diseases associated with abnormal kinase activity

INVENTOR(S): Lyons, John; Rubinfeld, Joseph

PATENT ASSIGNEE(S): SuperGen, Inc., USA

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003065995	A2	20030814	WO 2003-US3537	20030206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

Searched by Barb O'Bryen, STIC 571-272-2518

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,  
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,  
RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,  
NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,  
ML, MR, NE, SN, TD, TG

US 2003147813 A1 20030807 US 2002-71849 20020207  
PRIORITY APPLN. INFO.: US 2002-71849 A1 20020207  
US 2002-206854 A1 20020726

ED Entered STN: 15 Aug 2003

AB Methods are provided for treating diseases assocd. with abnormal activity of kinases such as chronic myelogenous leukemia. The method comprises: administering a DNA methylation inhibitor to the patient in therapeutically effective amt.; and administering a kinase inhibitor such as imatinib mesylate to the patient in therapeutically effective amt., such that the in vivo activity of the kinase is reduced relative to that prior to the treatment. The method can be used to treat cancer assocd. with abnormal activity of kinases such as phosphatidylinositol 3'-kinase (PI3K), protein kinases including serine/threonine kinases such as Raf kinases, protein kinase kinases such as MEK, and tyrosine kinases such as those in the epidermal growth factor receptor family (EGFR), platelet-derived growth factor receptor family (PDGFR), vascular endothelial growth factor receptor (VEGFR) family, nerve growth factor receptor family (NGFR), fibroblast growth factor receptor family (FGFR) insulin receptor family, ephrin receptor family, Met family, Ror family, c-kit family, Src family, Fes family, JAK family, Fak family, Btk family, Syk/ZAP-70 family, and Abl family.

IT **139691-76-2**, Raf mitogen-activated protein kinase kinase kinase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(Raf mitogen-activated protein kinase kinase; treatment of diseases assocd. with abnormal kinase activity with serine/threonine kinase **inhibitor** and DNA methylation **inhibitor**)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

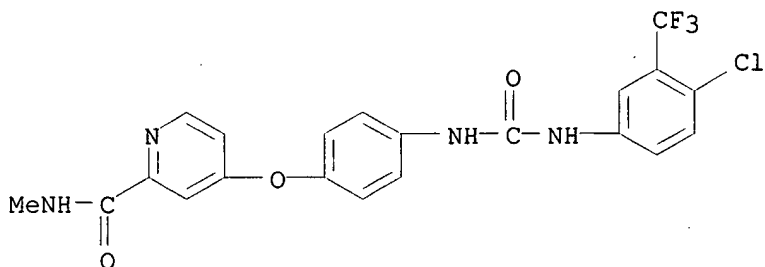
IT **284461-73-0**, BAY 43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of diseases assocd. with abnormal kinase activity with serine/threonine kinase inhibitor and DNA methylation inhibitor)

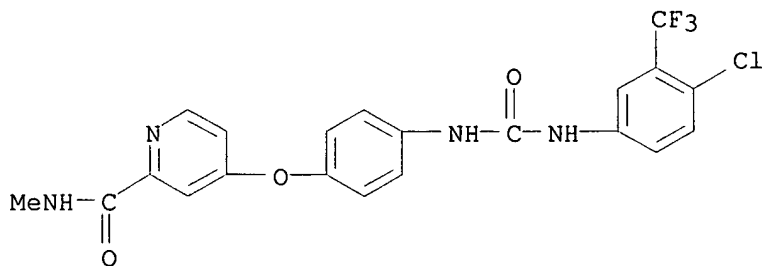
RN 284461-73-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



DOCUMENT NUMBER: 139:30782  
TITLE: RAF-MEK-ERK pathway inhibitors to treat cancer  
INVENTOR(S): Lyons, John F.; Bollag, Gideon  
PATENT ASSIGNEE(S): Onyx Pharmaceuticals, Inc., USA  
SOURCE: PCT Int. Appl., 17 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003047523	A2	20030612	WO 2002-US38402	20021203
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003125359	A1	20030703	US 2002-308721	20021203
PRIORITY APPLN. INFO.:			US 2001-336886P	P 20011204
ED	Entered STN: 13 Jun 2003			
AB	Materials and methods for treating certain cancers are described, preferably cancers that result from the up-regulation of the RAF-MEK-ERK pathway, and more preferably chronic myelogenous leukemia, and which cancer is preferably resistant to the inhibitor of Bcr-Abl tyrosine kinase, imatinib.			
IT	284461-73-0, BAY 43-9006			
	RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (BAY 43-9006; RAF-MEK-ERK pathway inhibitors to treat cancer)			
RN	284461-73-0 CAPLUS			
CN	2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)			



IT 139691-76-2, Raf kinase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(RAF-MEK-ERK pathway inhibitors to treat cancer)  
RN 139691-76-2 CAPLUS  
CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

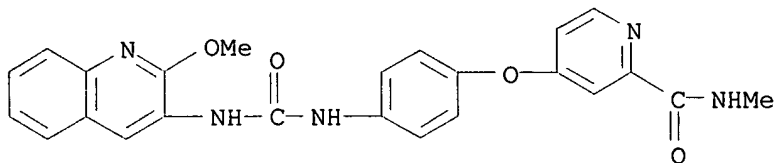
L122 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2003:874973 CAPLUS



DOCUMENT NUMBER: 139:364831  
TITLE: Preparation of quinolyl, isoquinolyl or pyridyl ureas as inhibitors of raf kinase using  
INVENTOR(S): Dumas, Jacques; Riedl, Bernd; Khire, Uday; Sibley, Robert N.; Hatoum-Mokdad, Holia; Monahan, Mary-Katherine; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.  
PATENT ASSIGNEE(S): Bayer Corporation, USA  
SOURCE: U.S. Pat. Appl. Publ., 26 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003207914	A1	20031106	US 2002-125369	20020419
PRIORITY APPLN. INFO.:			US 2001-367376P	P 20010420

OTHER SOURCE(S): MARPAT 139:364831  
ED Entered STN: 07 Nov 2003  
AB Urea derivs. of general formula A-NHCONH-B, A'-CONH-B', and A''-NHCONH-B" or pharmaceutically acceptable salts thereof [wherein A = each (un)substituted tert-butylpyridyl, (trifluoromethyl)pyridyl, isopropylpyridyl, 2-methyl-2-butylpyridyl, or 3-methyl-3-pentylpyridyl; A' = each (un)substituted isoquinolinyl or isoquinolinyl; A" = substituted quinolinyl group; B, B' = independently, (un)substituted bridged cyclic structure of up to 30 carbon atoms of the formula -L-(ML1)q (wherein L comprises a cyclic moiety having at least 5 members and is bound directly to D; L1 comprises a cyclic moiety having at least 5 members; M is a bridging group having at least one atom, q is an integer of from 1-3, and each cyclic structure of L and L1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur); B" = (un)substituted up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with a cyclic structure bound directly to D contg. at least 5 members with 0-4 members of the group consisting of nitrogen, oxygen and sulfur] are prepd. These compds. are useful in treating raf-mediated diseases, in particular cancerous cell growth mediated by a raf kinase. All compds. exemplified, e.g. N-(4-tert-Butylpyridyl)-N'-(2,3-dichlorophenyl)urea, displayed IC50 of between 10 nM and 10 .mu.M against ref kinase.  
IT 139691-76-2, Raf Kinase  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (prepn. of quinolyl, isoquinolyl or pyridyl ureas as inhibitors of raf kinase)  
RN 139691-76-2 CAPLUS  
CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)  
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
IT 432050-22-1P, N-(2-Methoxy-3-quinolinyl)-N'-[4-[2-(N-Methylcarbamyl)-4-pyridyloxy]phenyl]urea  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of quinolyl, isoquinolyl or pyridyl ureas as inhibitors of raf kinase)  
RN 432050-22-1 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



L122 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:874965 CAPLUS

DOCUMENT NUMBER: 139:364958

TITLE: Preparation of omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors

INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 60 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003207872	A1	20031106	US 2002-42226	20020111
PRIORITY APPLN. INFO.:			US 2002-42226	20020111

OTHER SOURCE(S): MARPAT 139:364958

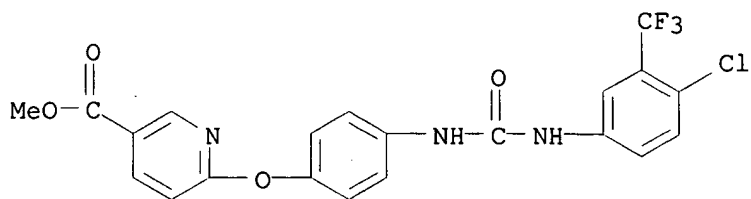
ED Entered STN: 07 Nov 2003

AB Urea derivs. of formula A-NHCONH-B or pharmaceutically acceptable salts thereof [A = a substituted moiety of up to 40 carbon atoms of the formula -L-(M-L1)q; where L = a 5 or 6 membered cyclic structure bound directly to D; L1 = a substituted cyclic moiety having at least 5 members; M = a bridging group having at least one atom; q = an integer of 1-3; each cyclic structure of L and L1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur; B = a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D contg. 0-4 members of the group consisting of nitrogen, oxygen and sulfur] are prepd. These compds. are useful for raf mediated diseases, in particular a cancerous cell growth mediated by raf kinase. All compds. exemplified, e.g. N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea, displayed IC50 of between 1 mM and 10 .mu.M.

IT 604813-15-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[3-(5-methoxycarbonylpyridyl)oxy]phenyl]urea 620963-02-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(3-methoxycarbonylphenyl)carboxyaminophenyl]urea 620963-04-4P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(3-methylcarbamoylphenyl)carboxyaminophenyl]urea  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (intermediate; prepn. of .omega.-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)

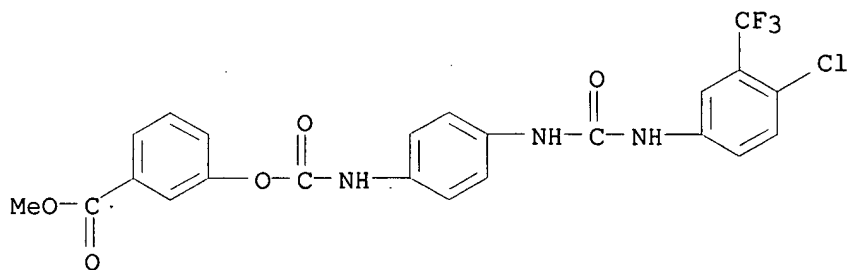
RN 604813-15-2 CAPLUS

CN 3-Pyridinecarboxylic acid, 6-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
 (CA INDEX NAME)



RN 620963-02-2 CAPLUS

CN Benzoic acid, 3-[[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]amino]carbonyloxy]-, methyl ester (9CI) (CA INDEX NAME)



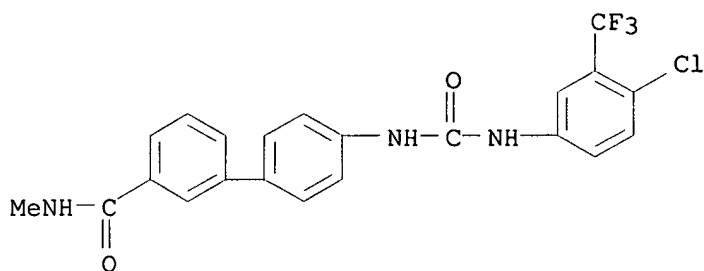
RN 620963-04-4 CAPLUS

CN Carbamic acid, compd. with 4'-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-N-methyl[1,1'-biphenyl]-3-carboxamide (1:1) (9CI) (CA INDEX NAME)

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CRN 620963-03-3

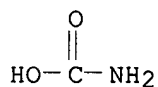
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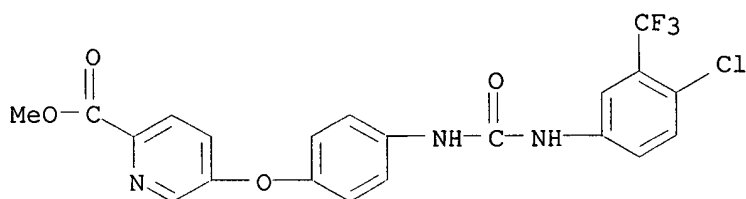
CM 2

CRN 463-77-4

CMF C H3 N O2

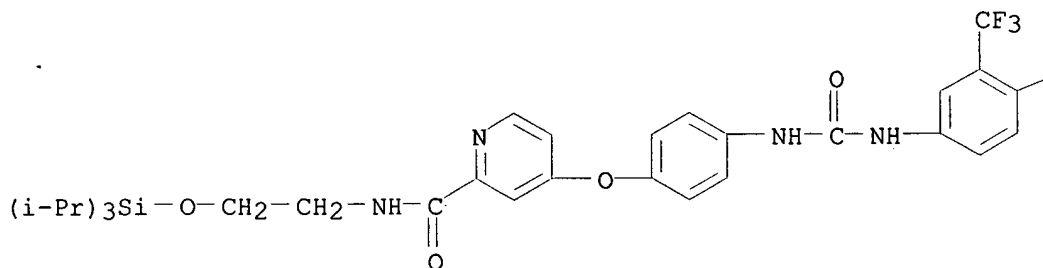


IT 284461-86-5P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(methoxycarbonyl)-5-pyridyloxy]phenyl]urea 284462-06-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-[N-(2-triisopropylsilyloxyethyl)carbonyl]-4-pyridyl]oxy]phenyl]urea 284671-00-7P, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-[4-[3-(5-methoxycarbonylpyridyl)oxy]phenyl]urea  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (intermediate; prepn. of .omega.-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)  
 RN 284461-86-5 CAPLUS  
 CN 2-Pyridinecarboxylic acid, 5-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
 (CA INDEX NAME)



RN 284462-06-2 CAPLUS  
 CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-[tris(1-methylethyl)silyl]oxy]ethyl]- (9CI)  
 (CA INDEX NAME)

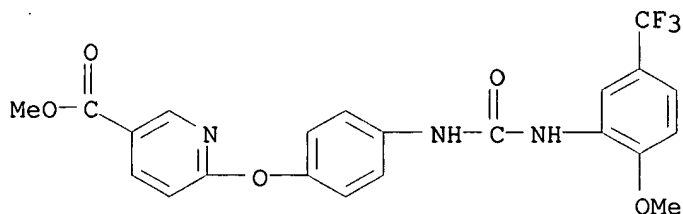
PAGE 1-A



PAGE 1-B

Cl

RN 284671-00-7 CAPLUS  
 CN 3-Pyridinecarboxylic acid, 6-[4-[[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
 (CA INDEX NAME)



IT 139691-76-2, Raf Kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(prepn. of .omega.-carboxyaryl substituted di-Ph ureas as raf kinase  
inhibitors for treating raf-mediated diseases such as cancerous  
cell growth)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 228418-48-2P 284461-33-2P 284461-34-3P  
284461-35-4P 284461-36-5P 284461-37-6P  
284461-40-1P 284461-41-2P 284461-42-3P  
284461-43-4P 284461-44-5P 284461-45-6P  
284461-46-7P 284461-47-8P 284461-48-9P  
284461-49-0P 284461-50-3P 284461-51-4P  
284461-52-5P 284461-53-6P 284461-55-8P  
284461-57-0P 284461-58-1P 284461-60-5P  
284461-61-6P 284461-62-7P 284461-63-8P  
284461-64-9P 284461-65-0P 284461-66-1P  
284461-67-2P 284461-68-3P 284461-70-7P  
284461-71-8P 284461-72-9P 284461-73-0P  
284461-74-1P 284461-75-2P 284461-76-3P  
284461-78-5P 284461-79-6P 284461-80-9P  
284461-81-0P 284461-82-1P 284461-83-2P  
284461-84-3P 284461-85-4P 284461-88-7P  
284461-89-8P 284461-90-1P 284461-91-2P  
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284462-31-3P 284462-34-6P 284462-35-7P,  
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284462-70-0P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[N-[3-  
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, N,N'-Bis[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea  
447457-08-1P 573673-43-5P 604813-02-7P  
604813-04-9P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[[3-[5-  
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620962-97-2P 620962-98-3P 620962-99-4P  
620963-00-0P

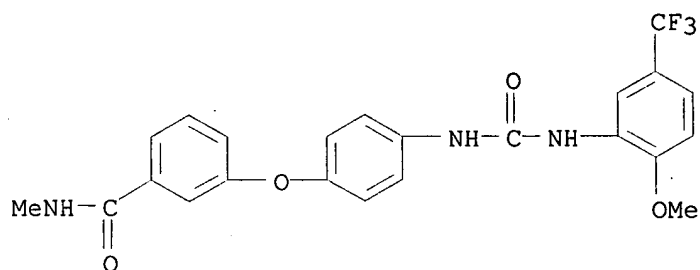
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

## (Uses)

(prepn. of .omega.-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)

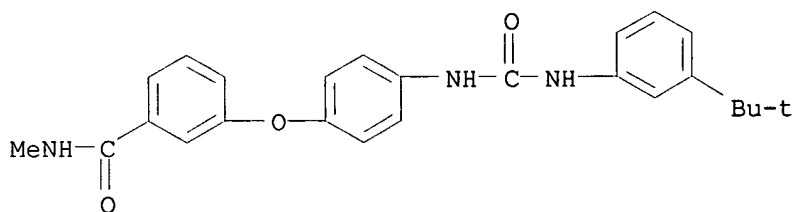
RN 228418-48-2 CAPLUS

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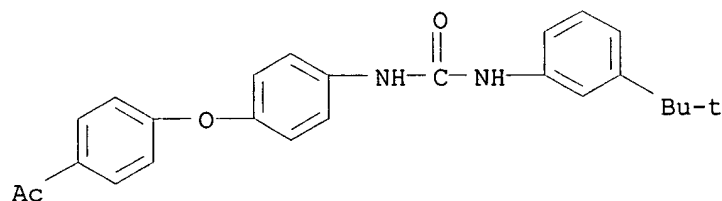
RN 284461-33-2 CAPLUS

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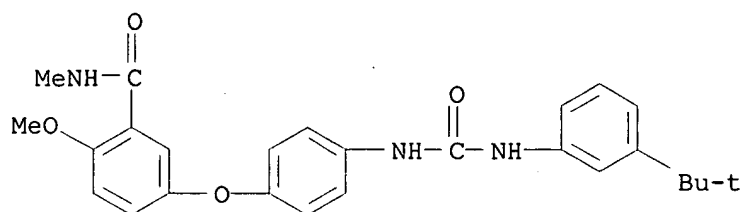
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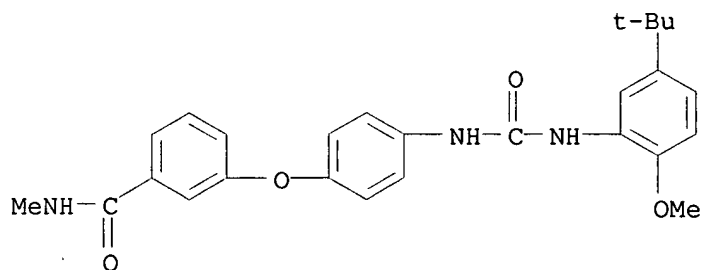
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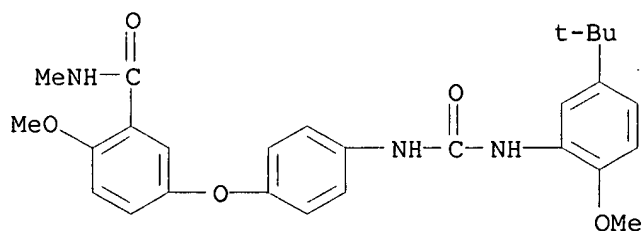
RN 284461-36-5 CAPLUS

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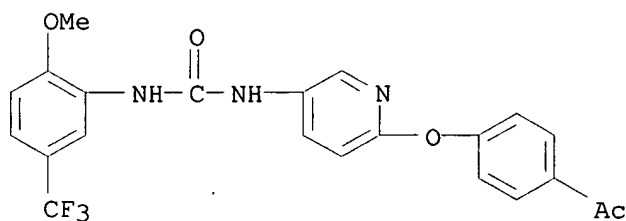
RN 284461-37-6 CAPLUS

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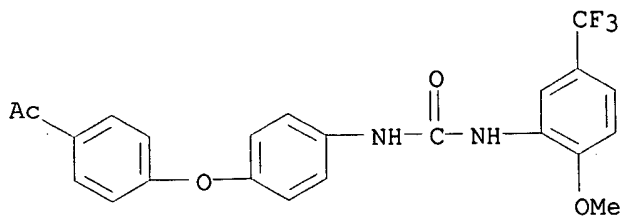
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CN Urea, N-[6-(4-acetylphenoxy)-3-pyridinyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

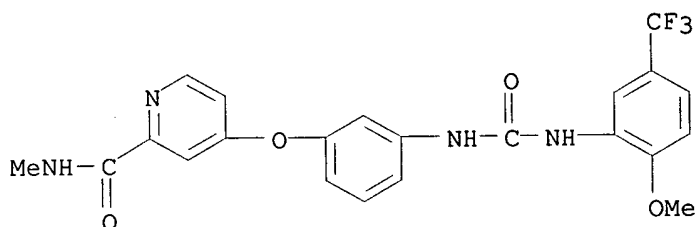


RN 284461-41-2 CAPLUS

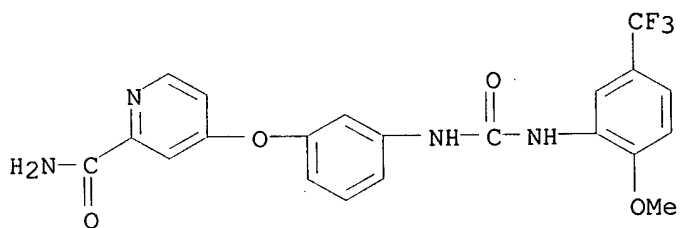
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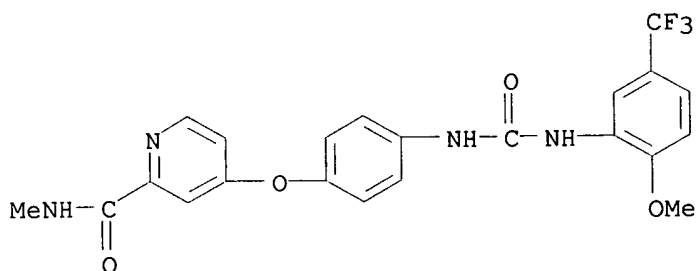
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CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-43-4 CAPLUS  
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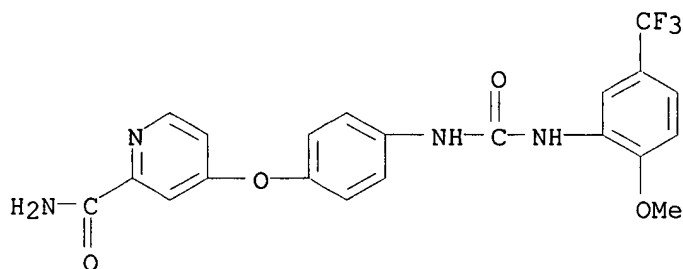


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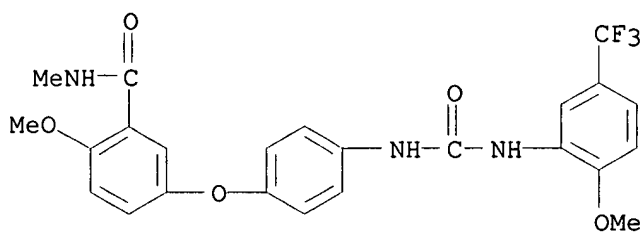


RN 284461-45-6 CAPLUS  
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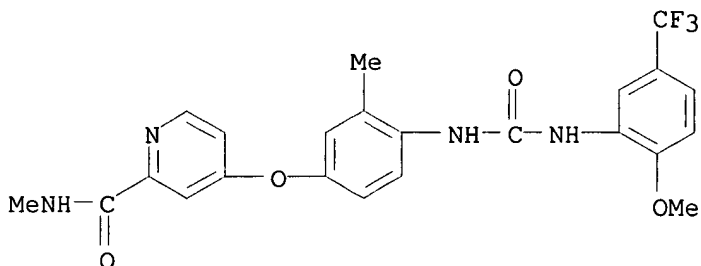




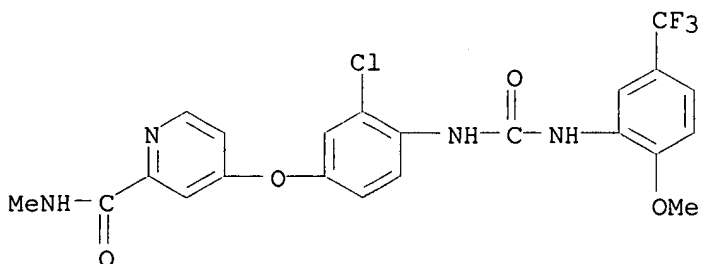
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RN 284461-47-8 CAPLUS  
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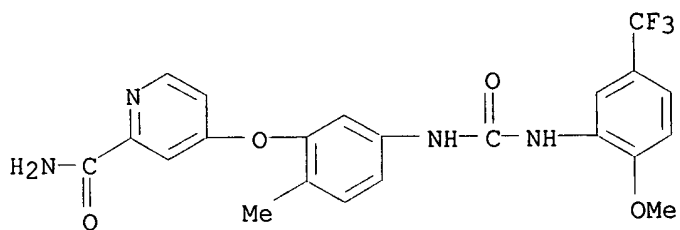


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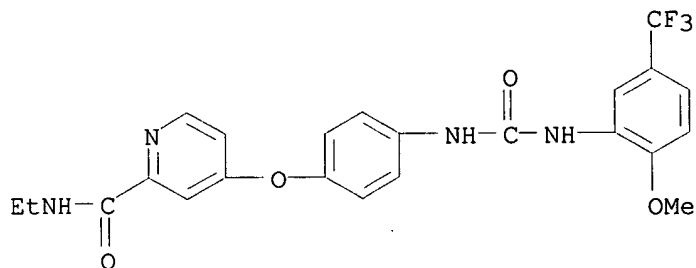
RN 284461-49-0 CAPLUS

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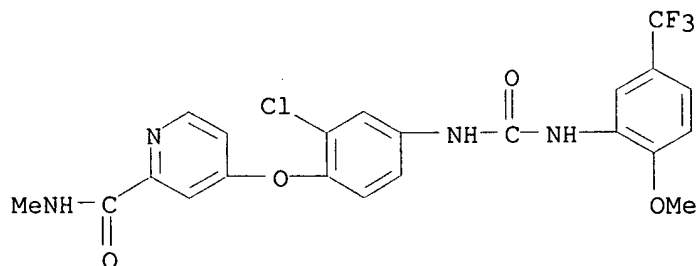
RN 284461-50-3 CAPLUS

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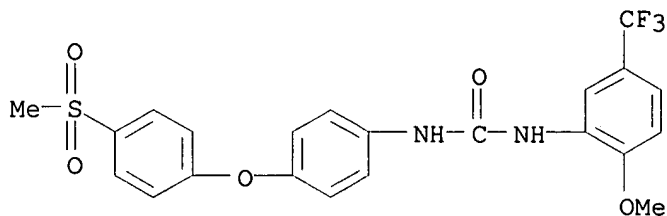
RN 284461-51-4 CAPLUS

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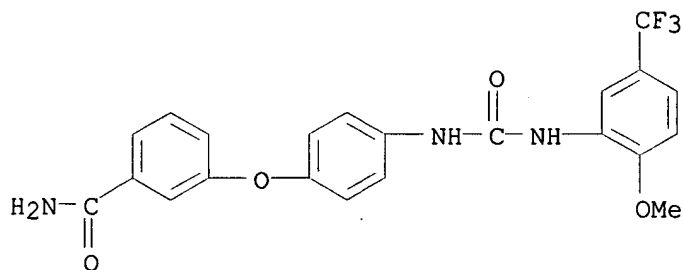
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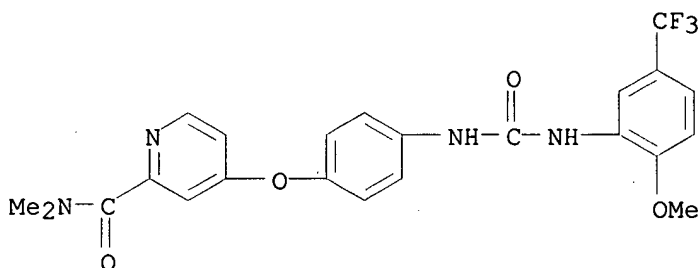
RN 284461-53-6 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



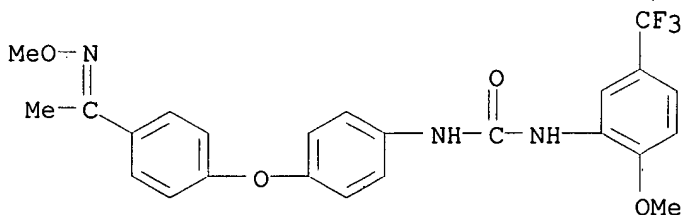
RN 284461-55-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



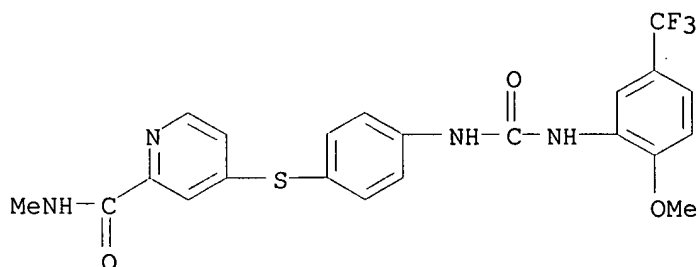
RN 284461-57-0 CAPLUS

CN Urea, N-[4-[4-[1-(methoxyimino)ethyl]phenoxy]phenyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

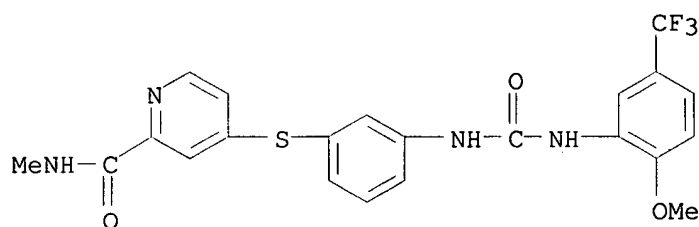


RN 284461-58-1 CAPLUS

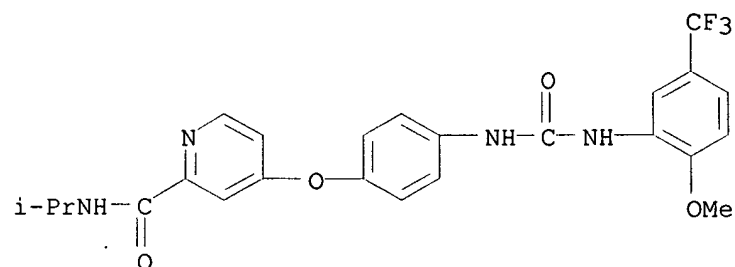
CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



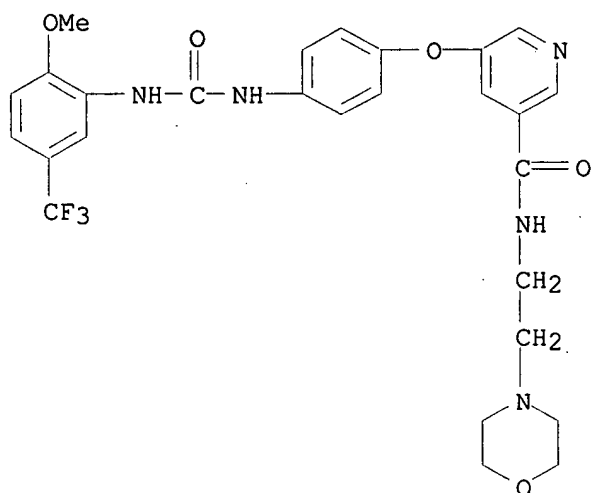
RN 284461-60-5 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-61-6 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

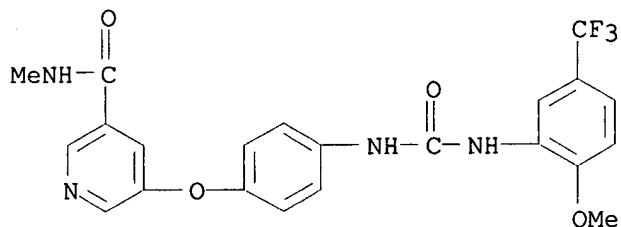


RN 284461-62-7 CAPLUS  
CN 3-Pyridinecarboxamide, 5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



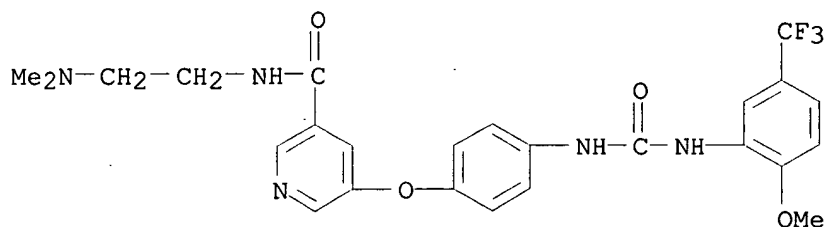
RN 284461-63-8 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



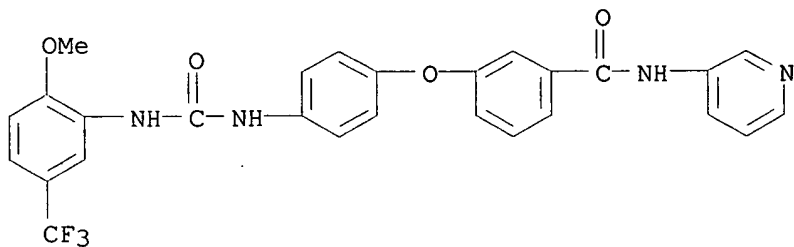
RN 284461-64-9 CAPLUS

CN 3-Pyridinecarboxamide, N-[2-(dimethylamino)ethyl]-5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



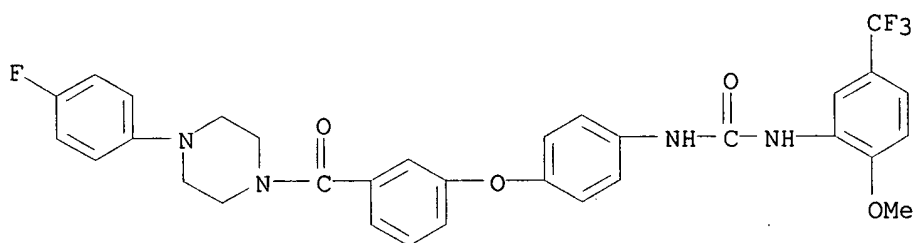
RN 284461-65-0 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-3-pyridinyl- (9CI) (CA INDEX NAME)



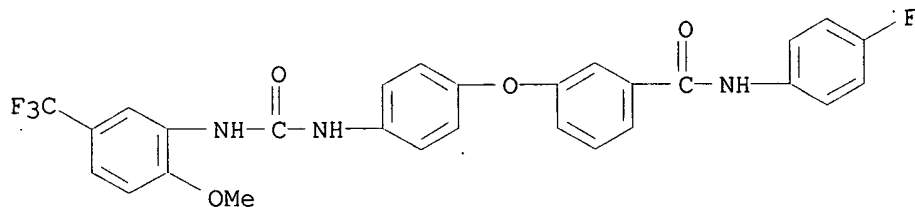
RN 284461-66-1 CAPLUS

CN Piperazine, 1-(4-fluorophenyl)-4-[3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]benzoyl]- (9CI) (CA INDEX NAME)



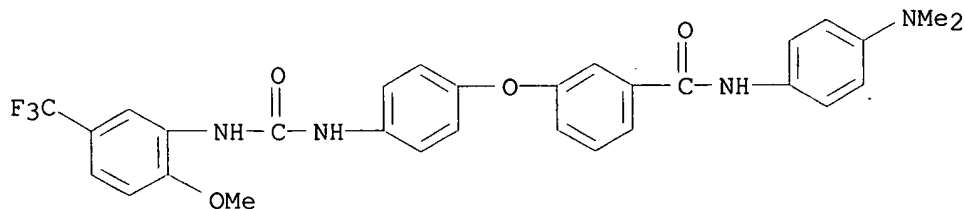
RN 284461-67-2 CAPLUS

CN Benzamide, N-(4-fluorophenyl)-3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



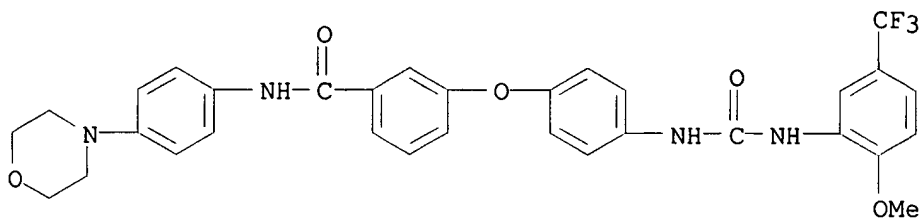
RN 284461-68-3 CAPLUS

CN Benzamide, N-[4-(dimethylamino)phenyl]-3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



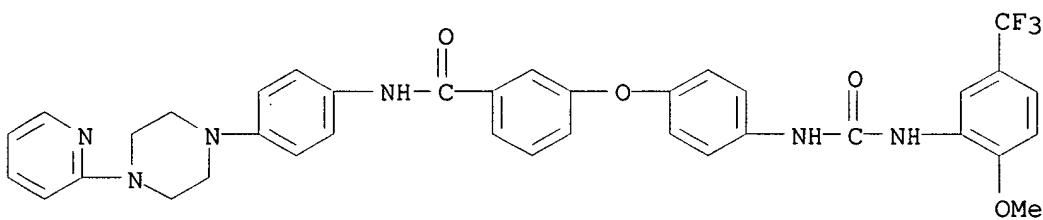
RN 284461-70-7 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



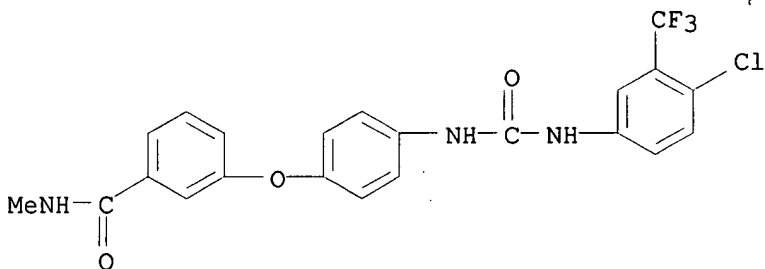
RN 284461-71-8 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-[4-(2-pyridinyl)-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



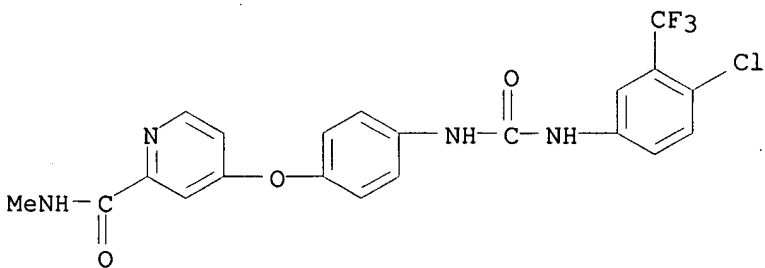
RN 284461-72-9 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-73-0 CAPLUS

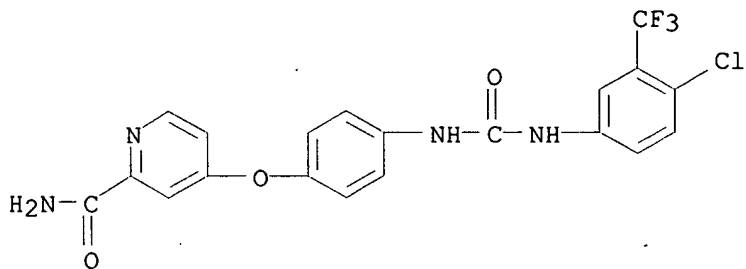
CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-74-1 CAPLUS

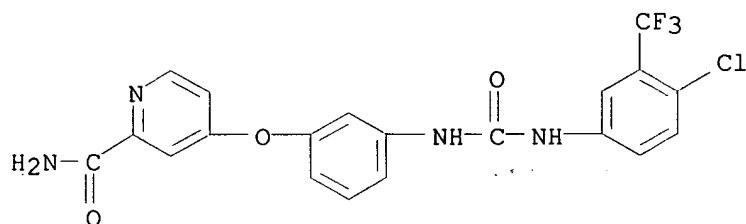
CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

arbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



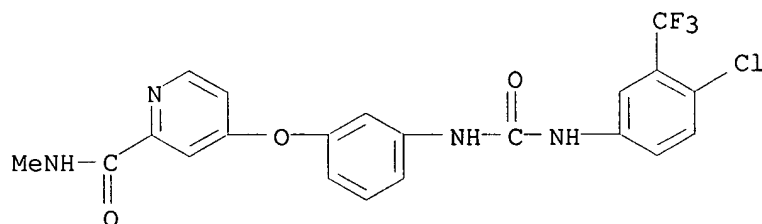
RN 284461-75-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



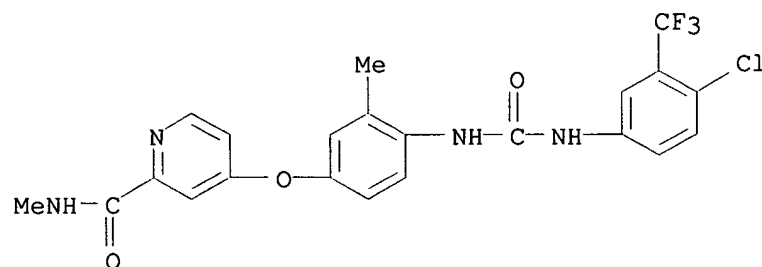
RN 284461-76-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-78-5 CAPLUS

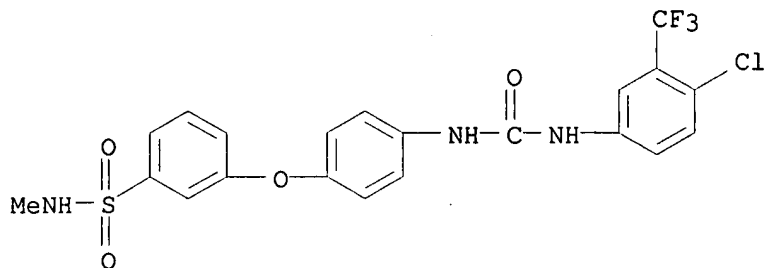
CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-3-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-79-6 CAPLUS

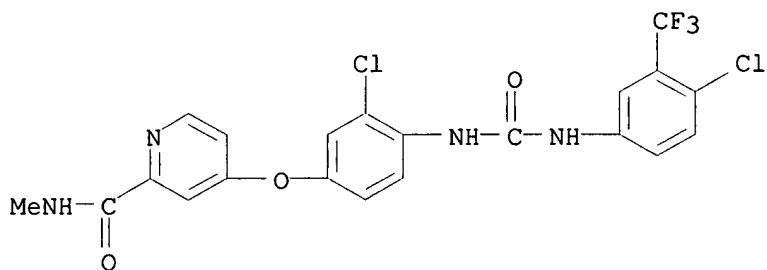


CN Benzenesulfonamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



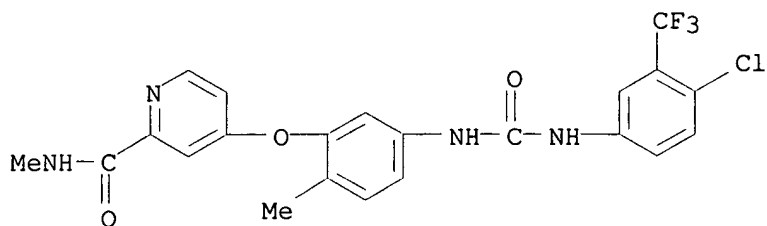
RN 284461-80-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-chloro-4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



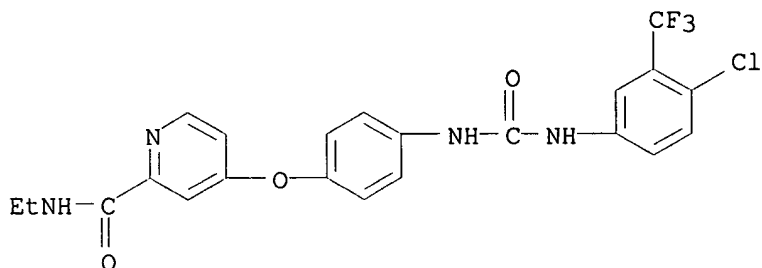
RN 284461-81-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)

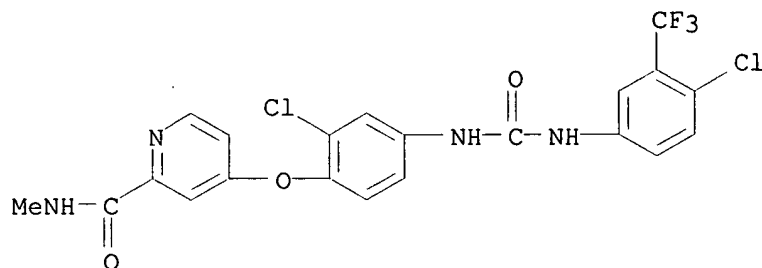


RN 284461-82-1 CAPLUS

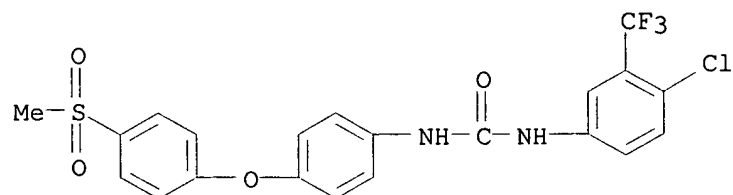
CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-ethyl- (9CI) (CA INDEX NAME)



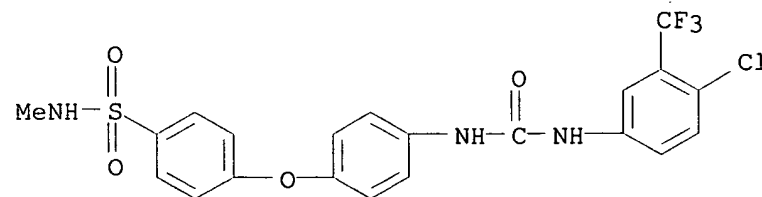
RN 284461-83-2 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[2-chloro-4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



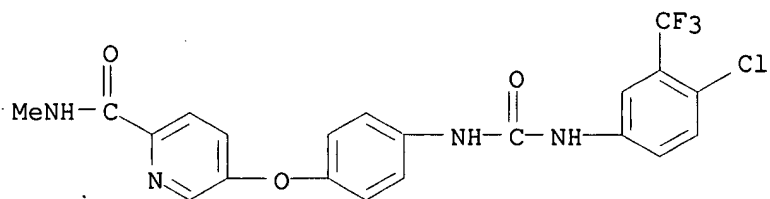
RN 284461-84-3 CAPLUS  
CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[4-(methylsulfonyl)phenoxy]phenyl]- (9CI) (CA INDEX NAME)



RN 284461-85-4 CAPLUS  
CN Benzenesulfonamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

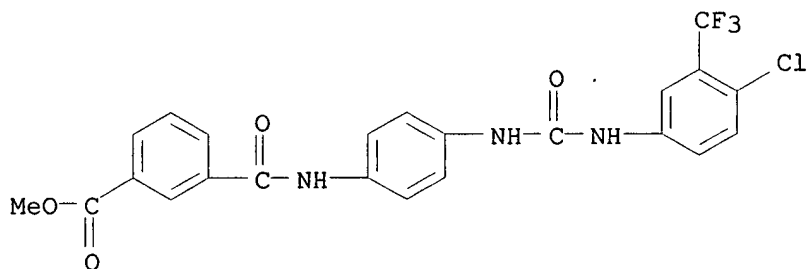


RN 284461-88-7 CAPLUS  
CN 2-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



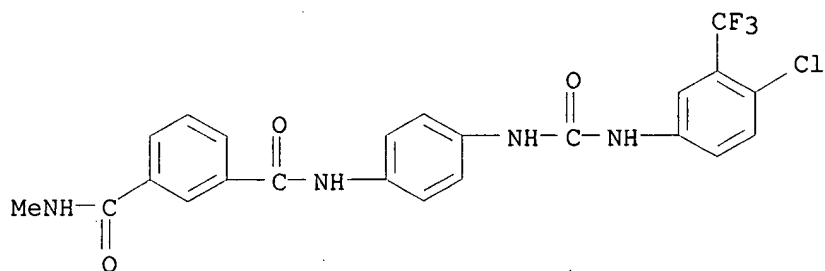
RN 284461-89-8 CAPLUS

CN Benzoic acid, 3-[[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



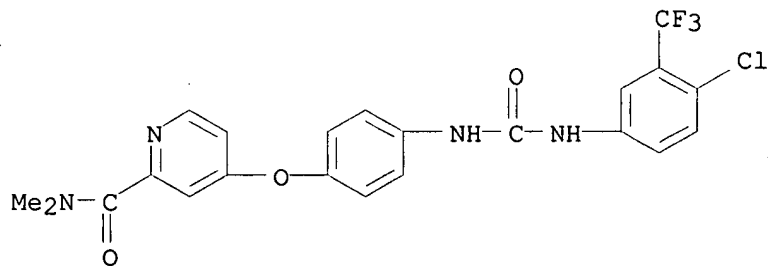
RN 284461-90-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]-N'-methyl- (9CI) (CA INDEX NAME)



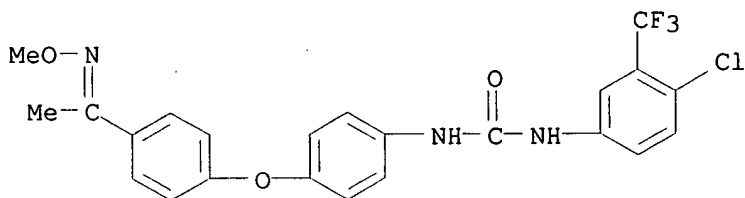
RN 284461-91-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



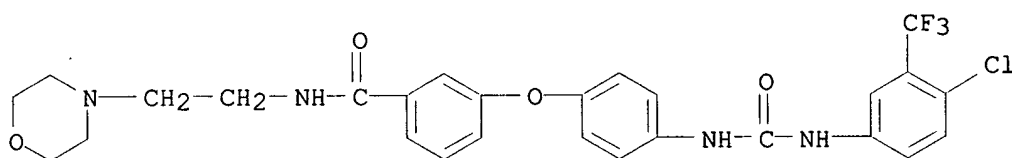
RN 284461-92-3 CAPLUS

CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[4-[1-(methoxyimino)ethyl]phenoxy]phenyl]- (9CI) (CA INDEX NAME)



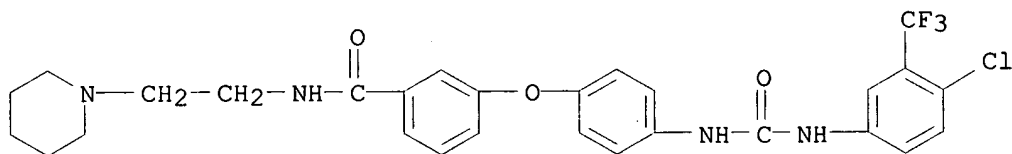
RN 284461-93-4 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



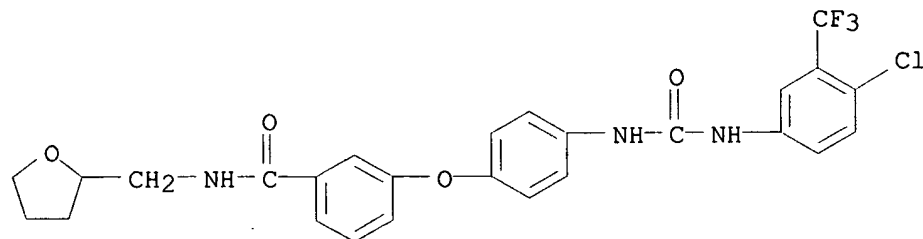
RN 284461-94-5 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



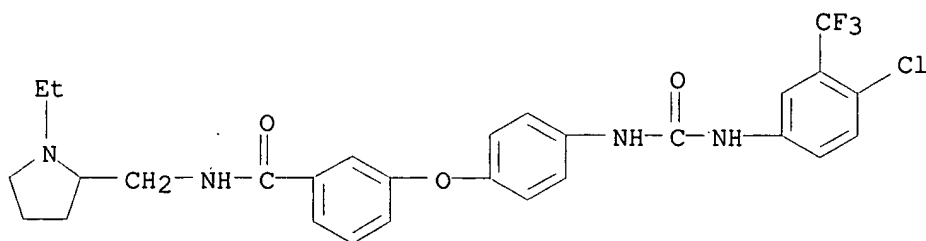
RN 284461-95-6 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



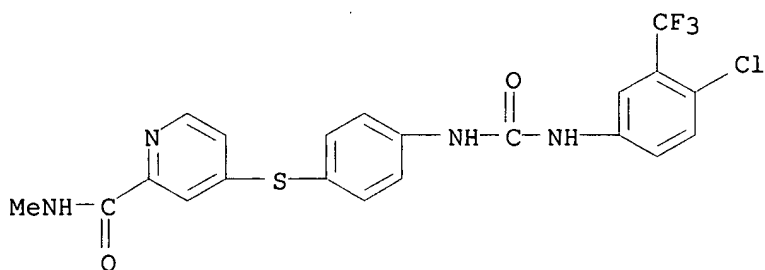
RN 284461-96-7 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[(1-ethyl-2-pyrrolidinyl)methyl]- (9CI) (CA INDEX NAME)



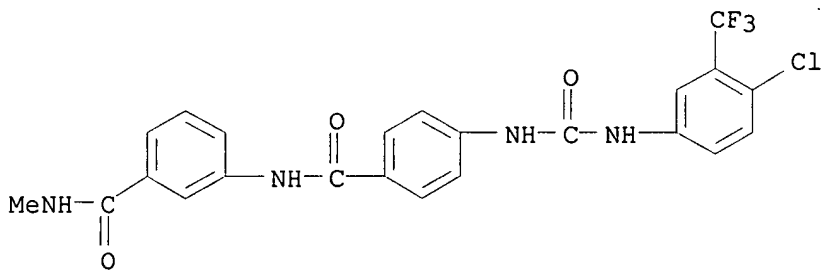
RN 284461-97-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



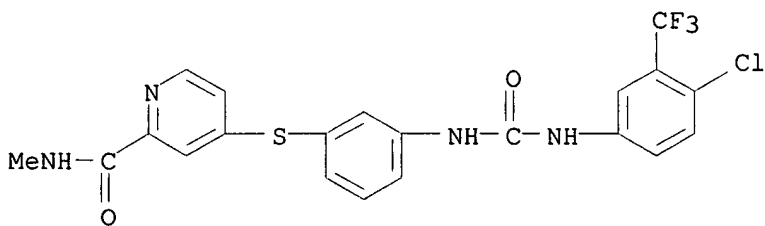
RN 284461-99-0 CAPLUS

CN Benzamide, 3-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]benzoyl]amino]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-01-7 CAPLUS

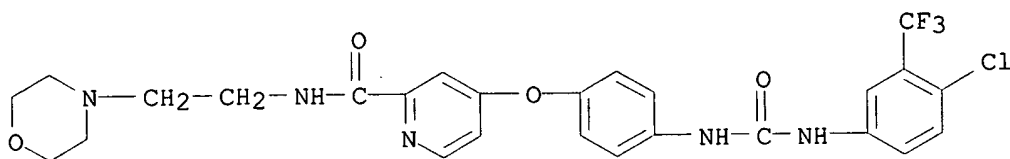
CN 2-Pyridinecarboxamide, 4-[[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-02-8 CAPLUS

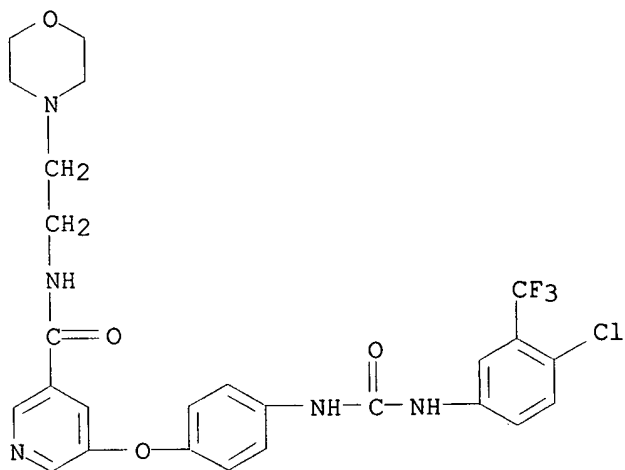
CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)

carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



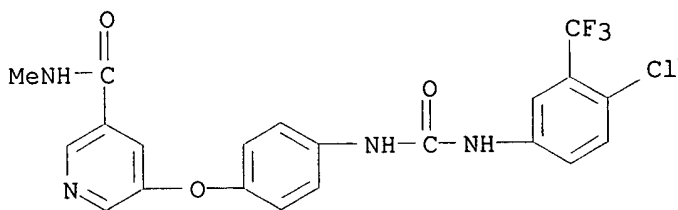
RN 284462-03-9 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



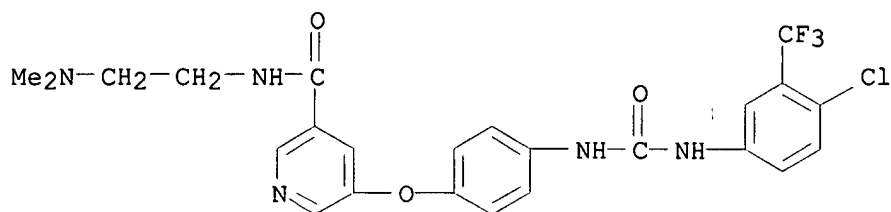
RN 284462-04-0 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



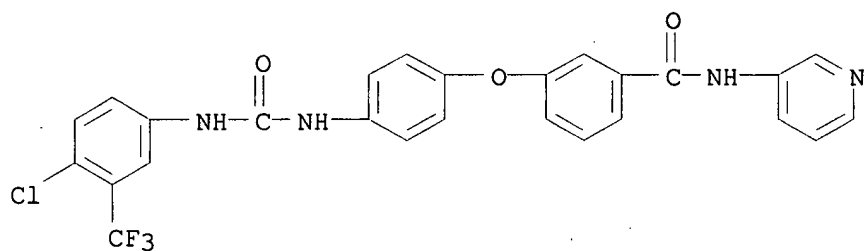
RN 284462-05-1 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



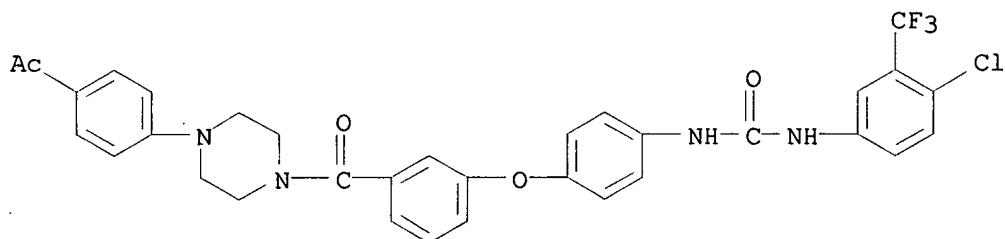
RN 284462-07-3 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-3-pyridinyl- (9CI) (CA INDEX NAME)



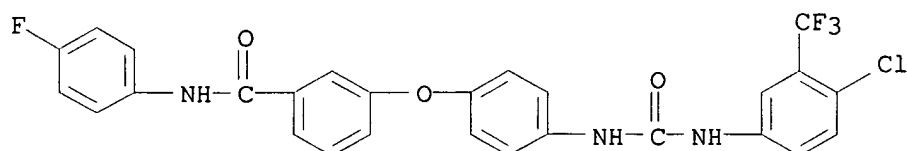
RN 284462-08-4 CAPLUS

CN Piperazine, 1-(4-acetylphenyl)-4-[3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]benzoyl]- (9CI) (CA INDEX NAME)



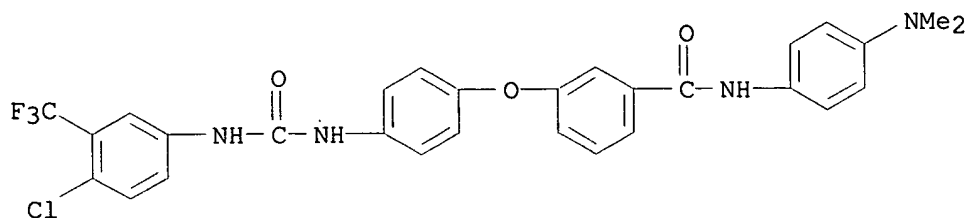
RN 284462-09-5 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



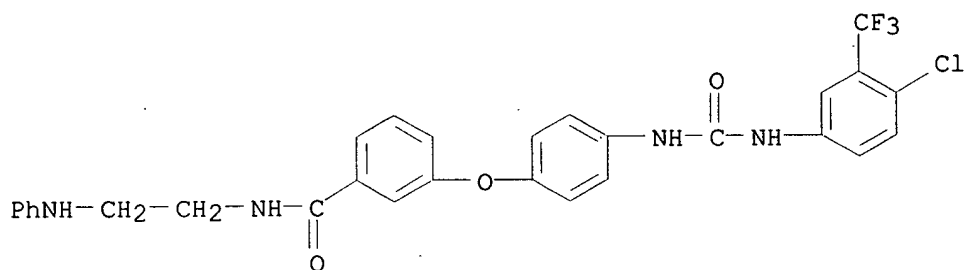
RN 284462-10-8 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-(dimethylamino)phenyl]- (9CI) (CA INDEX NAME)



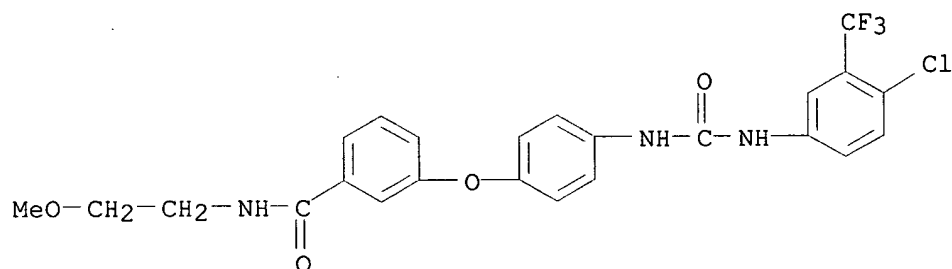
RN 284462-11-9 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(phenylamino)ethyl]- (9CI) (CA INDEX NAME)



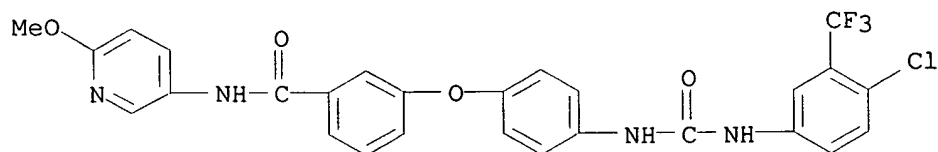
RN 284462-12-0 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(2-methoxyethyl)- (9CI) (CA INDEX NAME)



RN 284462-13-1 CAPLUS

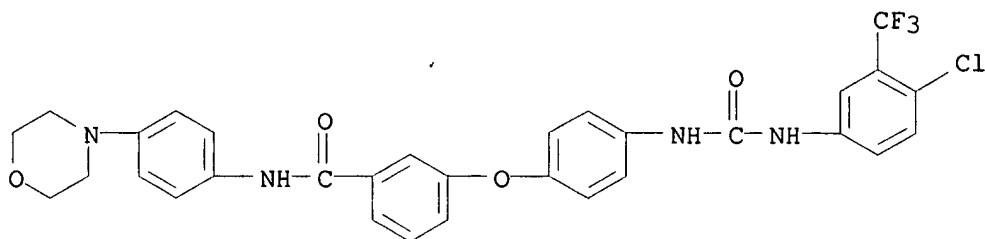
CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(6-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 284462-15-3 CAPLUS

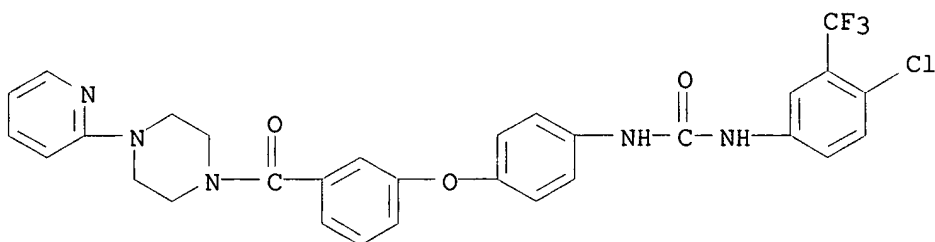
CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)





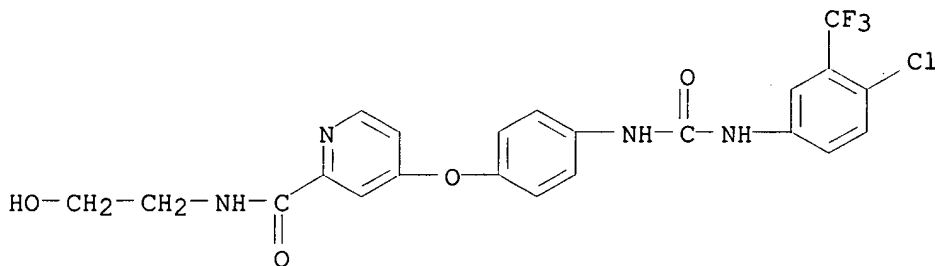
RN 284462-16-4 CAPLUS

CN Piperazine, 1-[3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]benzoyl]-4-(2-pyridinyl)- (9CI) (CA INDEX NAME)



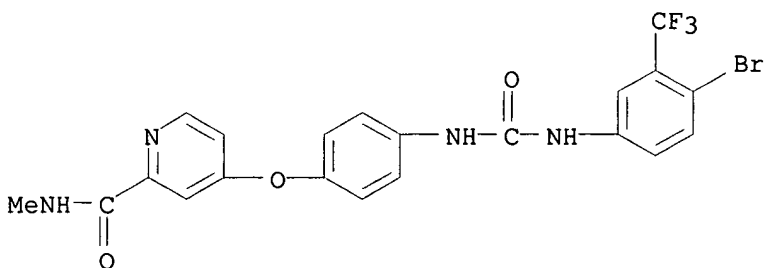
RN 284462-17-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



RN 284462-18-6 CAPLUS

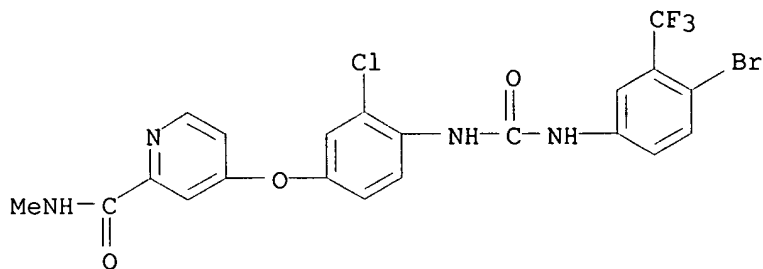
CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-19-7 CAPLUS

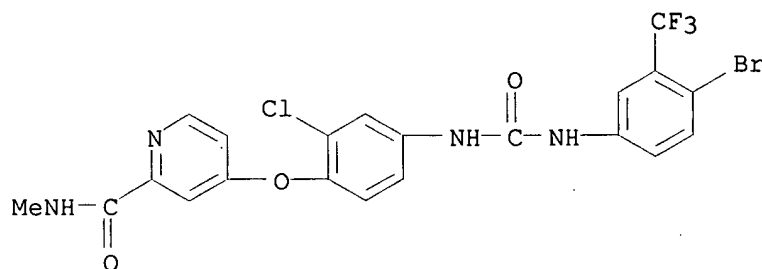
CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

rbonyl]amino]-3-chlorophenoxy]-N-methyl- (9CI) (CA INDEX NAME)



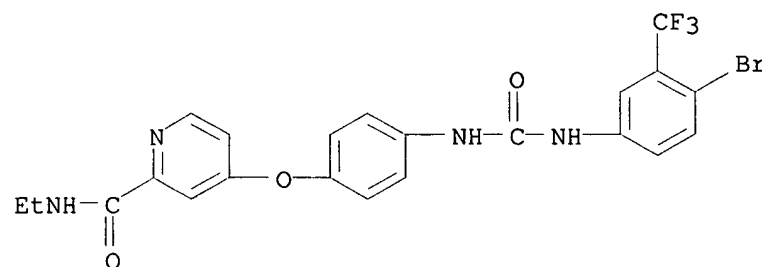
RN 284462-20-0 CAPLUS

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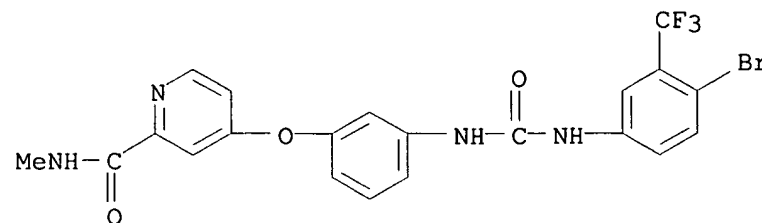
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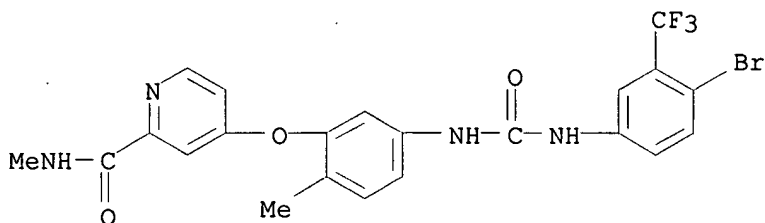


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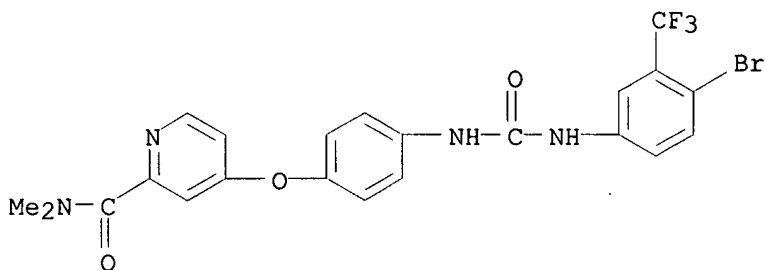
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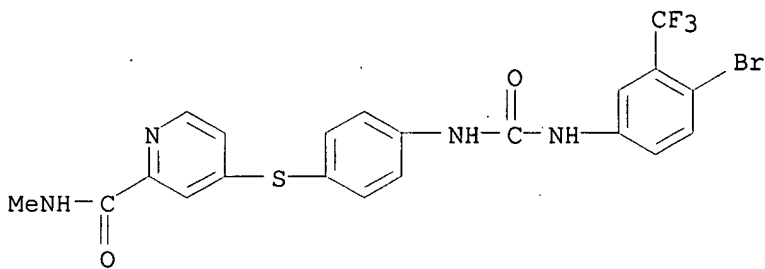
RN 284462-23-3 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



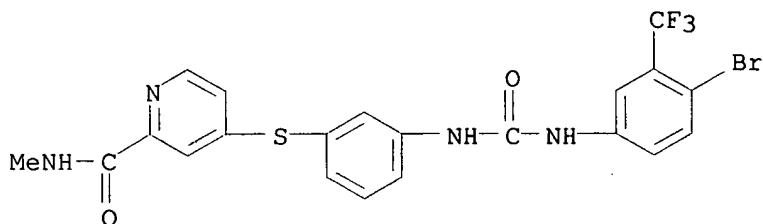
RN 284462-24-4 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 284462-25-5 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)

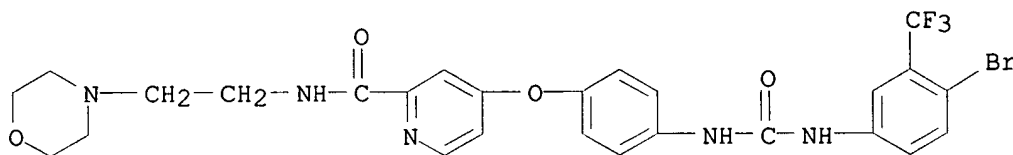


RN 284462-26-6 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



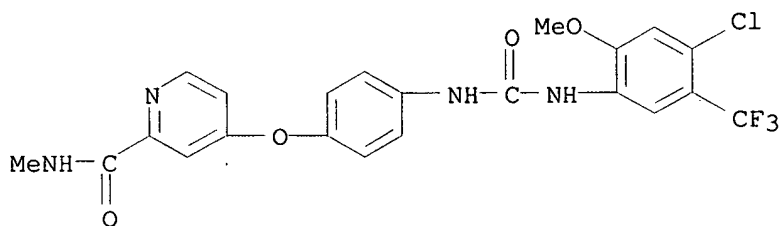
RN 284462-27-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



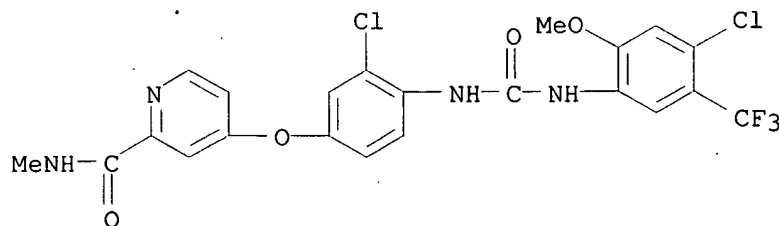
RN 284462-28-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



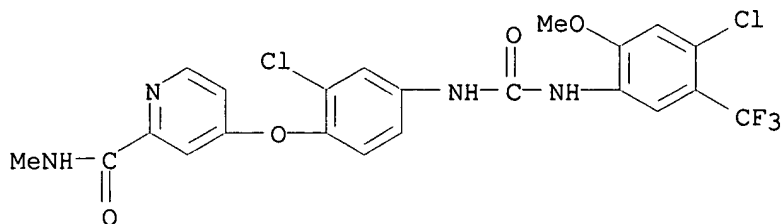
RN 284462-29-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-chloro-4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



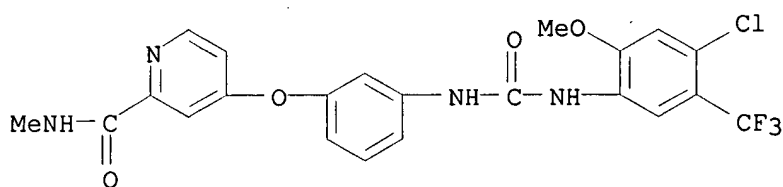
RN 284462-30-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[2-chloro-4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



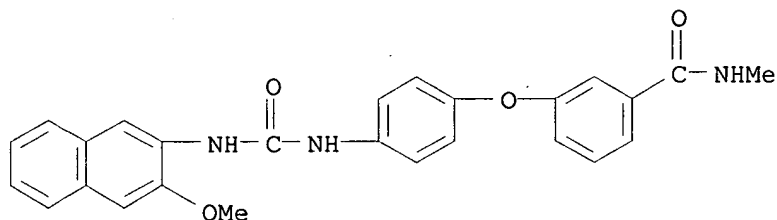
RN 284462-31-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



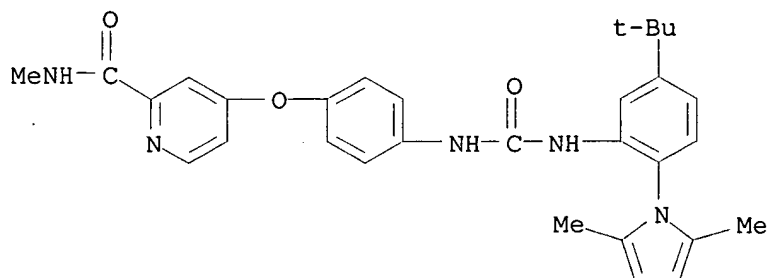
RN 284462-34-6 CAPLUS

CN Benzamide, 3-[4-[[[3-methoxy-2-naphthalenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



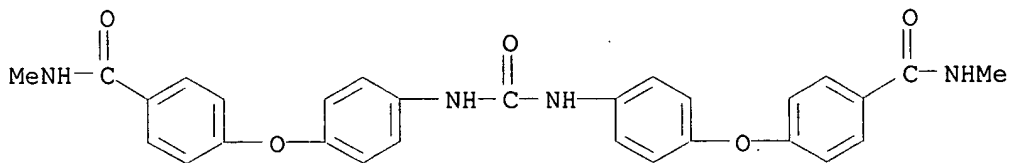
RN 284462-35-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[5-(1,1-dimethylethyl)-2-(2,5-dimethyl-1H-pyrrol-1-yl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



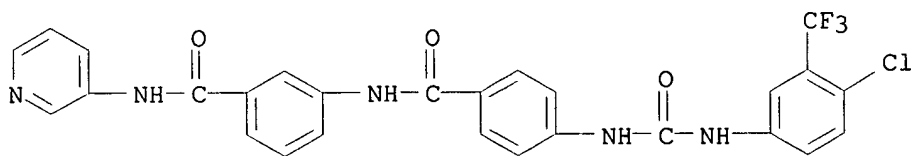
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CN Benzamide, 4,4'-[carbonylbis(imino-4,1-phenyleneoxy)]bis[N-methyl- (9CI) (CA INDEX NAME)]



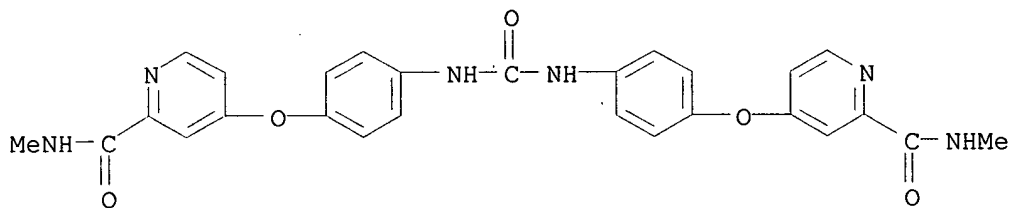
RN 284462-70-0 CAPLUS

CN Benzamide, 3-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]benzoyl]amino]-N-3-pyridinyl- (9CI) (CA INDEX NAME)



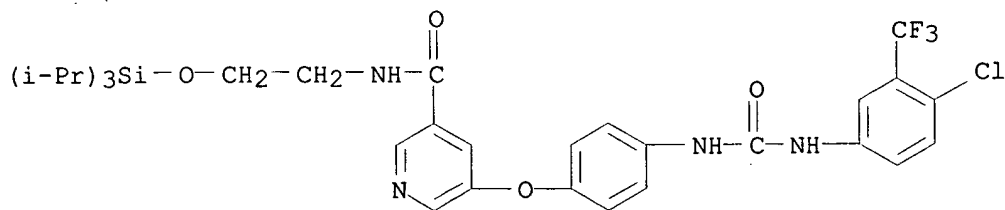
RN 284670-98-0 CAPLUS

CN 2-Pyridinecarboxamide, 4,4'-[carbonylbis(imino-4,1-phenyleneoxy)]bis[N-methyl- (9CI) (CA INDEX NAME)



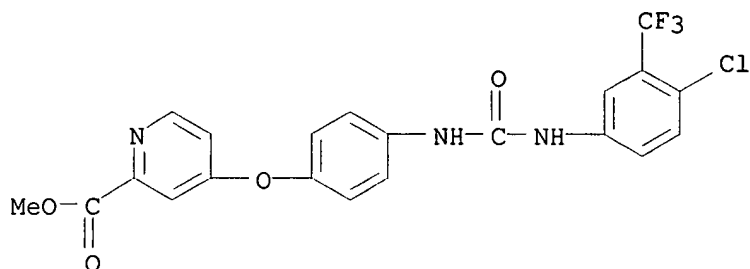
RN 447457-08-1 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-[[tris(1-methylethyl)silyl]oxy]ethyl]- (9CI) (CA INDEX NAME)



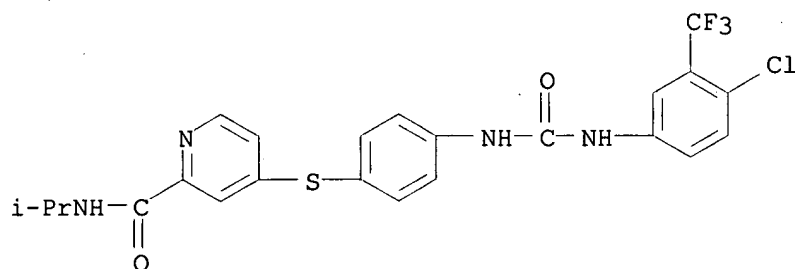
RN 573673-43-5 CAPLUS

CN 2-Pyridinecarboxylic acid, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)



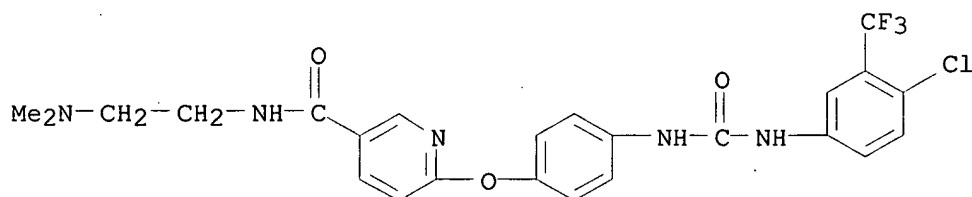
RN 604813-02-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



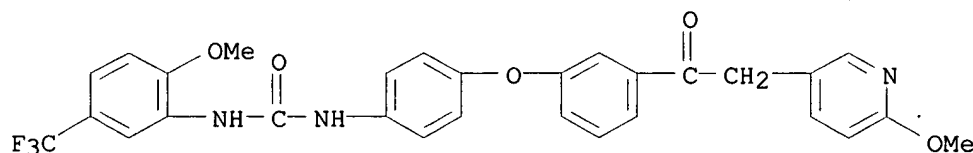
RN 604813-04-9 CAPLUS

CN 3-Pyridinecarboxamide, 6-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



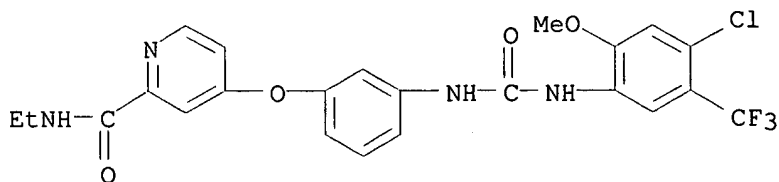
RN 620962-97-2 CAPLUS

CN Urea, N-[4-[3-[(6-methoxy-3-pyridinyl)acetyl]phenoxy]phenyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



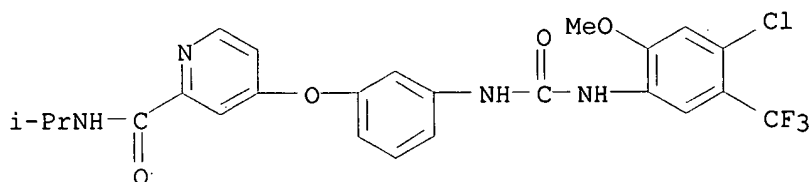
RN 620962-98-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-ethyl- (9CI) (CA INDEX NAME)



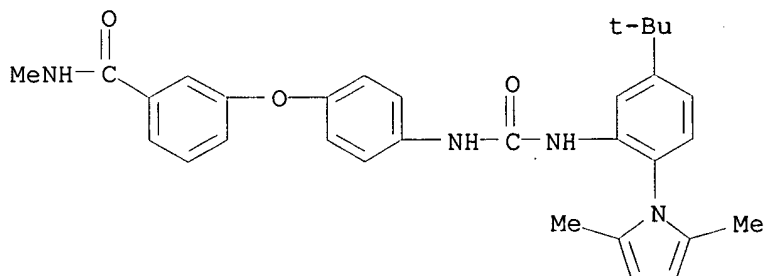
RN 620962-99-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 620963-00-0 CAPLUS

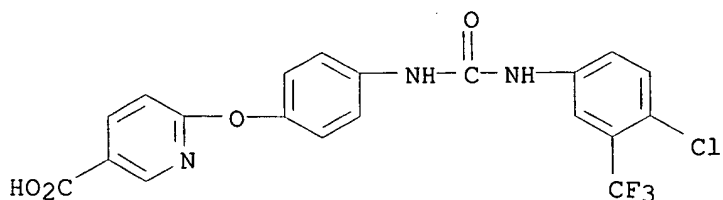
CN Benzamide, 3-[4-[[[5-(1,1-dimethylethyl)-2-(2,5-dimethyl-1H-pyrrol-1-yl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



IT 573673-47-9P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[3-(5-carboxypyridyl)oxy]phenyl]urea  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (reactant; prepn. of .omega.-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)

RN 573673-47-9 CAPLUS

CN 3-Pyridinecarboxylic acid, 6-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)





L122 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:757329 CAPLUS  
DOCUMENT NUMBER: 139:276918  
TITLE: Preparation of omega-carboxyaryl substituted diphenyl  
ureas as raf kinase inhibitors  
INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger,  
Timothy B.; Scott, William J.; Smith, Roger A.; Wood,  
Jill E.; Monahan, Mary-katherine; Natero, Reina;  
Renick, Joel; Sibley, Robert N.  
PATENT ASSIGNEE(S): Bayer Corporation, USA  
SOURCE: U.S. Pat. Appl. Publ., 61 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003181442	A1	20030925	US 2001-993647	2001/11/27
PRIORITY APPLN. INFO.:			US 2001-993647	2001/11/27
OTHER SOURCE(S):	MARPAT 139:276918			

ED Entered STN: 26 Sep 2003

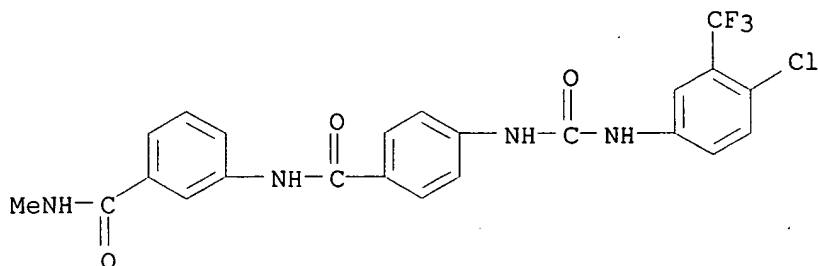
AB Aryl ureas of formula A-NHCONH-B [A = a substituted moiety of up to 40 carbon atoms of the formula: -L-(M-L1)q (where L = a 5 or 6 membered cyclic structure bound directly to D, L1 comprises a substituted cyclic moiety having at least 5 members; M = a bridging group having at least one atom; q = an integer of from 1-3; each cyclic structure of L and L1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur); B = a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D contg. 0-4 members of the group consisting of nitrogen, oxygen and sulfur] are prepd. These urea derivs. are useful for treating raf mediated diseases, in particular cancerous cell growth mediated by raf kinase. Thus, N-[4-bromo-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea. Thus, a soln. of 4-bromo-3-(trifluoromethyl)phenyl isocyanate (8.0 g, 30.1 mmol) in CH2Cl2 (80 mL) was added dropwise to a soln. of 4-[2-(N-methylcarbamoyl)-4-pyridyloxy]aniline (7.0 g, 28.8 mmol) in CH2Cl2 (40 mL) at 0.degree., stirred at room temp. for 16 h, and filtered to give, after washing the yellow solids, washing with CH2Cl2 (2 .times. 50 mL), and drying under reduced pressure (approx. 1 mmHg) at 40.degree. to give N-[4-bromo-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea. All compds. exemplified showed IC50 between 1 nM to 10 .mu.M against raf kinase.

IT **284461-99-0P**, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[(3-methylcarbamoylphenyl)carbamoyl]phenyl]urea **284670-98-0P**, N,N'-Bis[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(intermediate; prepn. of omega-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors and anticancer agents)

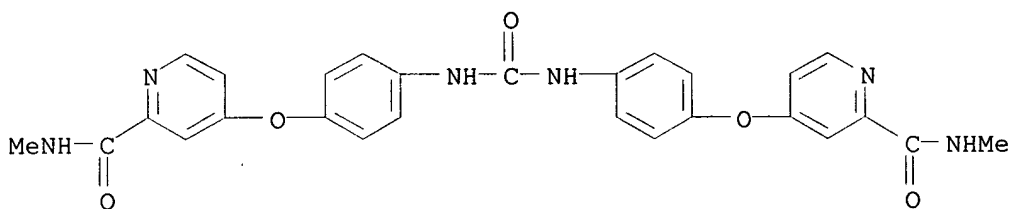
RN 284461-99-0 CAPLUS

CN Benzamide, 3-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]benzoyl]amino]-N-methyl- (9CI) (CA INDEX NAME)



RN 284670-98-0 CAPLUS

CN 2-Pyridinecarboxamide, 4,4'-[carbonylbis(imino-4,1-phenyleneoxy)]bis[N-methyl- (9CI) (CA INDEX NAME)]



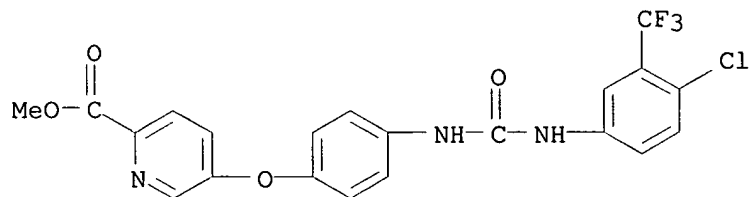
IT 284461-86-5P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[[2-(methoxycarbonyl)-5-pyridyl]oxy]phenyl]urea 284462-06-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-[N-(2-triisopropylsilyloxyethyl)carbonyl]-4-pyridyloxy]phenyl]urea 284462-71-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(5-carboxy-3-pyridyloxy)phenyl]urea 284462-76-6P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(5-methoxycarbonyl-3-pyridyloxy)phenyl]urea 284671-00-7P, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-[4-[3-(5-methoxycarbonylpyridyl)oxy]phenyl]urea 573673-59-3P, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-[4-(5-methoxycarbonyl-3-pyridyloxy)phenyl]urea 604813-15-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[3-(5-methoxycarbonylpyridyl)oxy]phenyl]urea

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; prepn. of omega-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors and anticancer agents)

RN 284461-86-5 CAPLUS

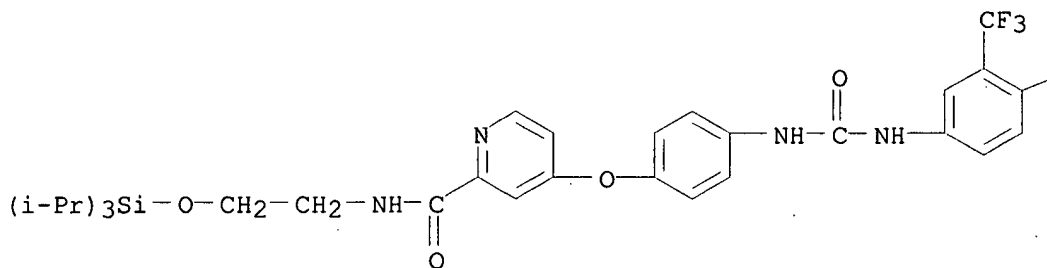
CN 2-Pyridinecarboxylic acid, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 284462-06-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-[[tris(1-methylethyl)silyl]oxy]ethyl]- (9CI) (CA INDEX NAME)

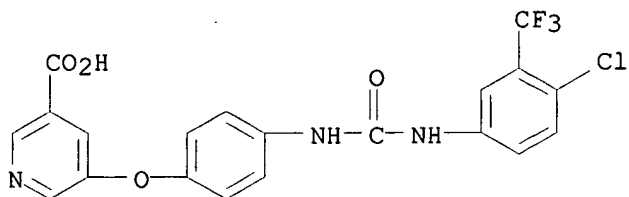
PAGE 1-A



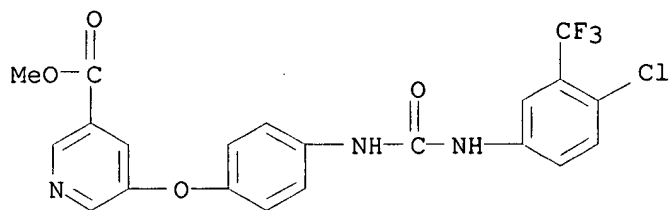
PAGE 1-B

Cl

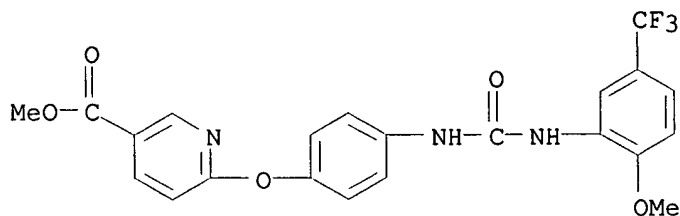
RN 284462-71-1 CAPLUS  
CN 3-Pyridinecarboxylic acid, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



RN 284462-76-6 CAPLUS  
CN 3-Pyridinecarboxylic acid, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
(CA INDEX NAME)

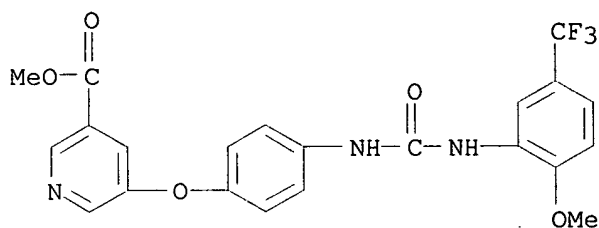


RN 284671-00-7 CAPLUS  
CN 3-Pyridinecarboxylic acid, 6-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
(CA INDEX NAME)



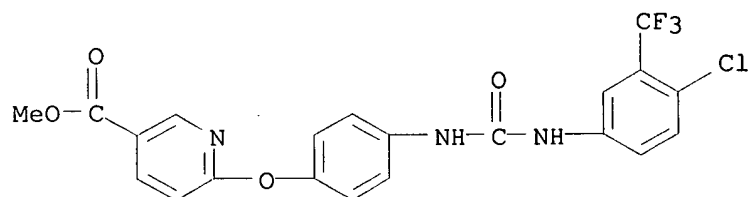
RN 573673-59-3 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
(CA INDEX NAME)



RN 604813-15-2 CAPLUS

CN 3-Pyridinecarboxylic acid, 6-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
(CA INDEX NAME)



IT 139691-76-2, Raf Kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(prepn. of omega-carboxyaryl substituted di-Ph ureas as raf kinase  
inhibitors and anticancer agents)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

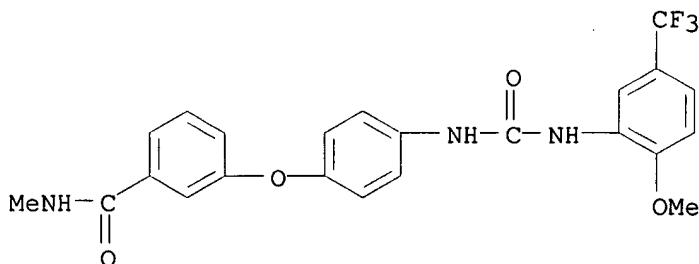
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284461-35-4P 284461-36-5P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[3-(methylcarbamoyl)phenoxy]phenyl]urea  
284461-37-6P 284461-40-1P 284461-41-2P  
284461-42-3P 284461-43-4P, N-(2-Methoxy-5-trifluoromethylphenyl)-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea  
284461-44-5P, N-(2-Methoxy-5-trifluoromethylphenyl)-N'-[4-[[2-(methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea 284461-45-6P,  
N-(2-Methoxy-5-trifluoromethylphenyl)-N'-[4-[(2-carbamoyl-4-pyridyl)oxy]phenyl]urea 284461-46-7P 284461-47-8P  
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trifluoromethylphenyl)-N'-[3-[(2-carbamoyl-4-pyridyl)oxy]-4-methylphenyl]urea 284461-50-3P 284461-51-4P  
284461-52-5P 284461-53-6P 284461-55-8P  
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284461-71-8P 284461-72-9P 284461-73-0P  
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284461-92-3P 284461-93-4P 284461-94-5P  
284461-95-6P 284461-96-7P 284461-97-8P  
284462-01-7P 284462-02-8P 284462-03-9P  
284462-04-0P 284462-05-1P 284462-07-3P  
284462-08-4P 284462-09-5P 284462-10-8P  
284462-11-9P 284462-12-0P 284462-13-1P  
284462-15-3P 284462-16-4P 284462-17-5P  
284462-18-6P 284462-19-7P 284462-20-0P  
284462-21-1P 284462-22-2P 284462-23-3P  
284462-24-4P 284462-25-5P 284462-26-6P  
284462-27-7P 284462-28-8P 284462-29-9P  
284462-30-2P 284462-31-3P 284462-32-4P  
284462-34-6P 284462-35-7P, N-[2-(2,5-Dimethyl-1-pyrrolyl)-5-tert-butylphenyl]-N'-[4-[(2-methylcarbamoyl-4-pyridyl)oxy]phenyl]urea 284462-36-8P 284462-70-0P,  
N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[N-[3-[N-(3-pyridyl)carbamoyl]phenyl]carbamoyl]phenyl]urea 447457-08-1P  
447457-09-2P 573673-43-5P 604813-02-7P  
604813-04-9P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[3-[5-[[2-(dimethylamino)ethyl]carbamoyl]pyridyl]oxy]phenyl]urea  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of omega-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors and anticancer agents)

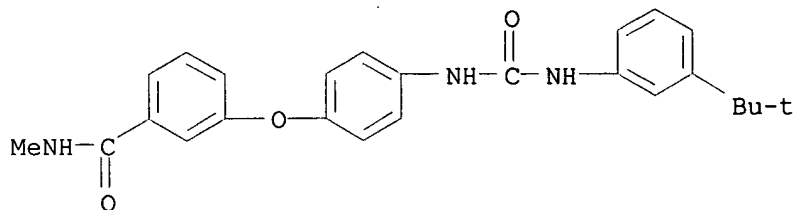
RN 228418-48-2 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

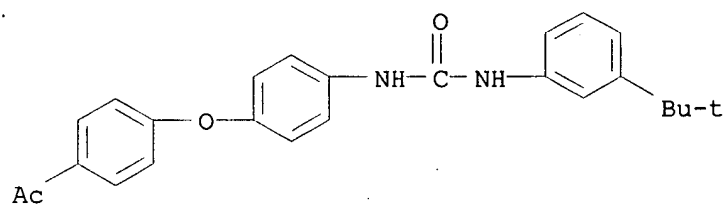


RN 284461-33-2 CAPLUS

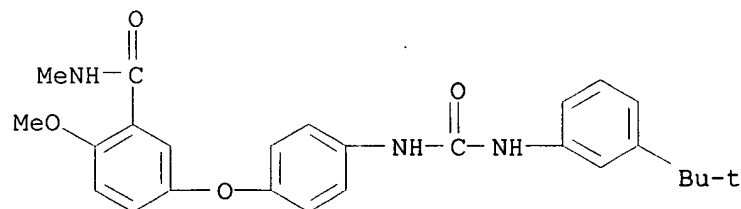
CN Benzamide, 3-[4-[[[3-(1,1-dimethylethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



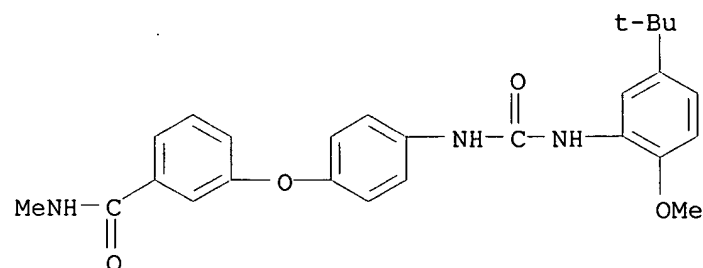
RN 284461-34-3 CAPLUS  
CN Urea, N-[4-(4-acetylphenoxy)phenyl]-N'-[3-(1,1-dimethylethyl)phenyl]- (9CI) (CA INDEX NAME)



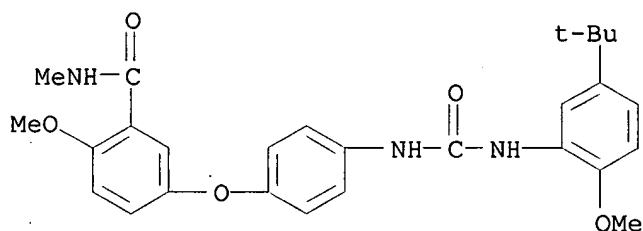
RN 284461-35-4 CAPLUS  
CN Benzamide, 5-[4-[[[3-(1,1-dimethylethyl)phenyl]amino]carbonyl]amino]phenoxy]-2-methoxy-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-36-5 CAPLUS  
CN Benzamide, 3-[4-[[[5-(1,1-dimethylethyl)-2-methoxyphenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

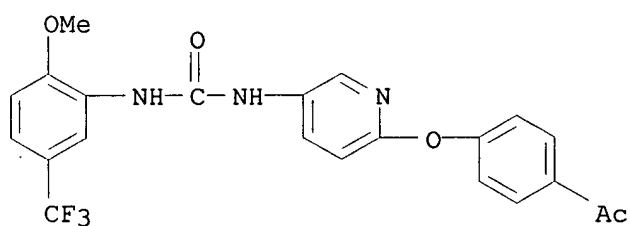


RN 284461-37-6 CAPLUS  
CN Benzamide, 5-[4-[[[5-(1,1-dimethylethyl)-2-methoxyphenyl]amino]carbonyl]amino]phenoxy]-2-methoxy-N-methyl- (9CI) (CA INDEX NAME)



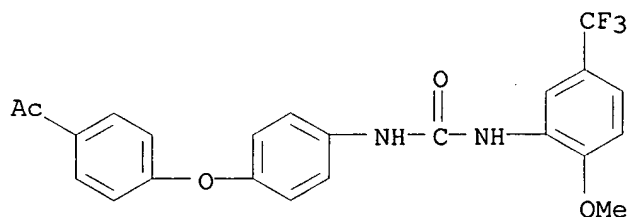
RN 284461-40-1 CAPLUS

CN Urea, N-[6-(4-acetylphenoxy)-3-pyridinyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



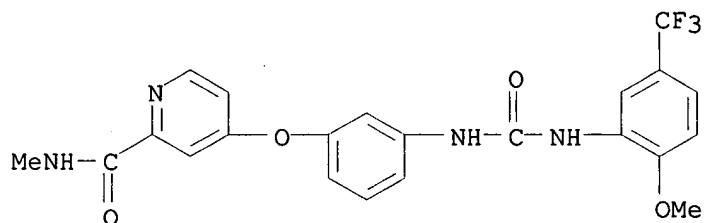
RN 284461-41-2 CAPLUS

CN Urea, N-[4-(4-acetylphenoxy)phenyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



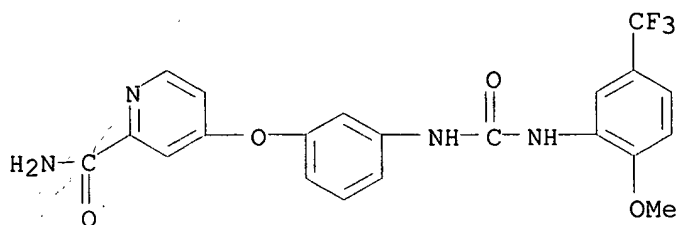
RN 284461-42-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



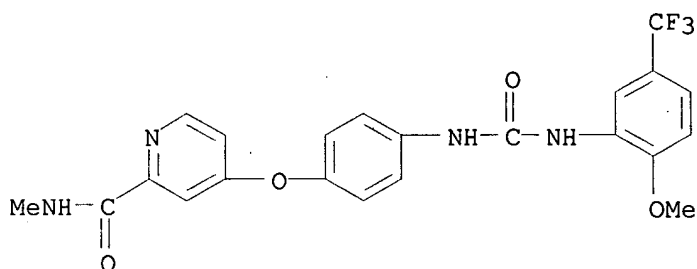
RN 284461-43-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



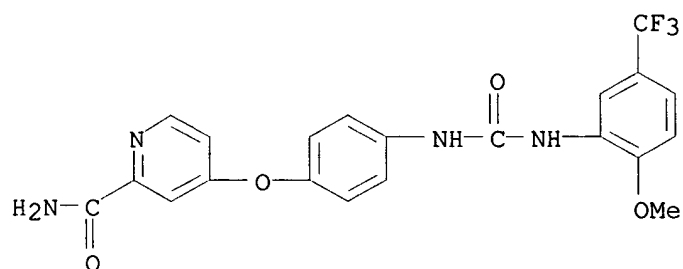
RN 284461-44-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



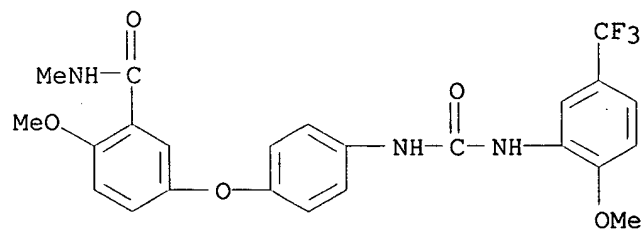
RN 284461-45-6 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



RN 284461-46-7 CAPLUS

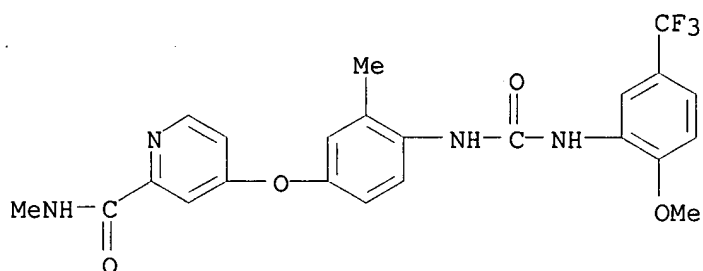
CN Benzamide, 2-methoxy-5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-47-8 CAPLUS

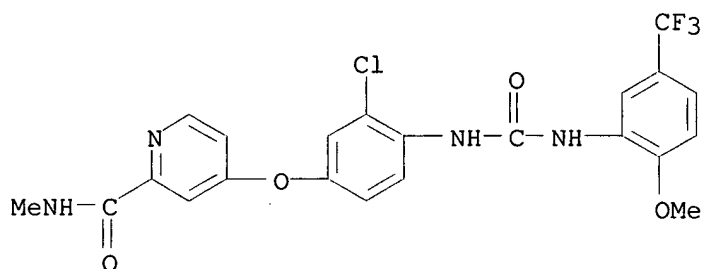
CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]-3-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)





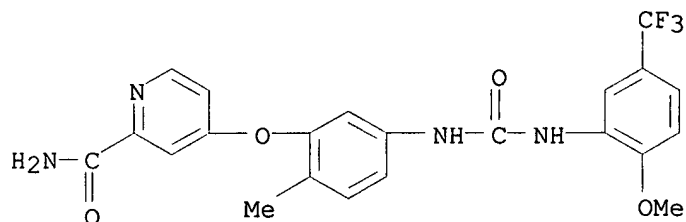
RN 284461-48-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-chloro-4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



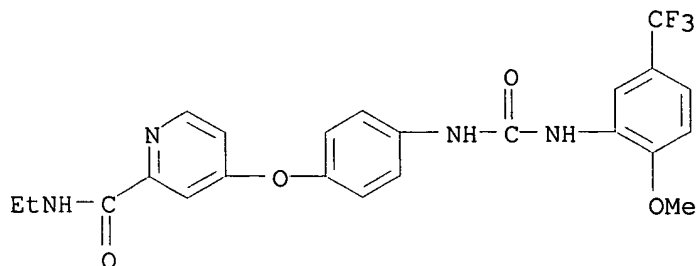
RN 284461-49-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]- (9CI) (CA INDEX NAME)

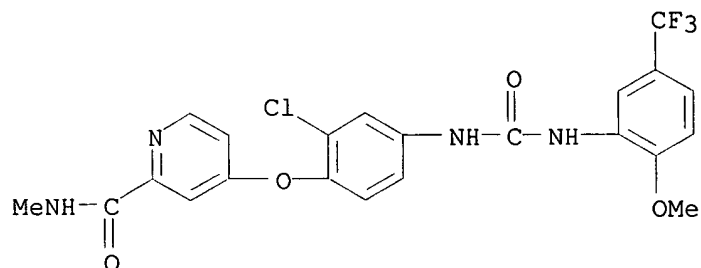


RN 284461-50-3 CAPLUS

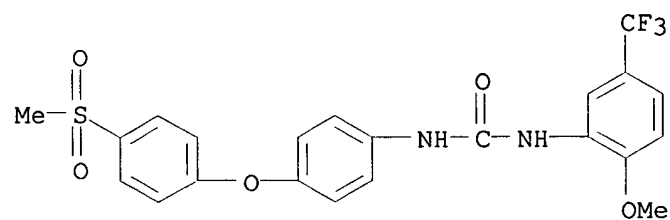
CN 2-Pyridinecarboxamide, N-ethyl-4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



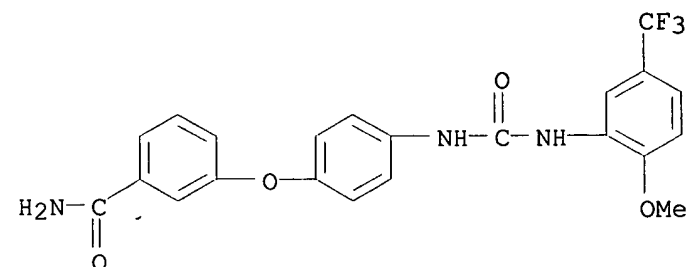
RN 284461-51-4 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[2-chloro-4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-52-5 CAPLUS  
CN Urea, N-[2-methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[4-(methylsulfonyl)phenoxy]phenyl]- (9CI) (CA INDEX NAME)

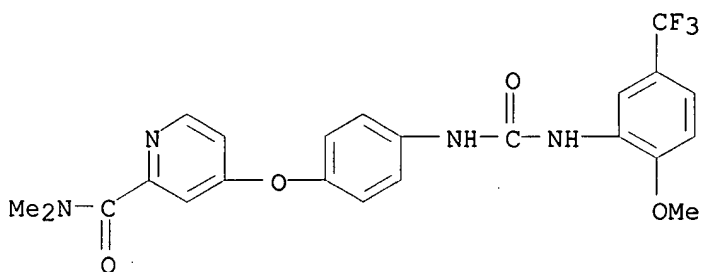


RN 284461-53-6 CAPLUS  
CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



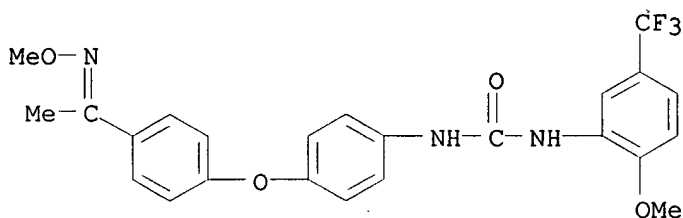
RN 284461-55-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



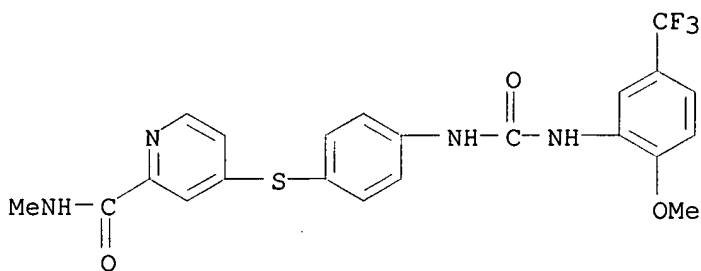
RN 284461-57-0 CAPLUS

CN Urea, N-[4-[4-[1-(methoxyimino)ethyl]phenoxy]phenyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



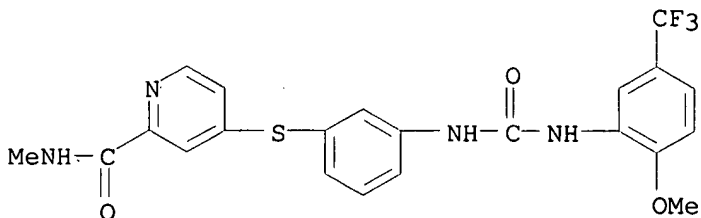
RN 284461-58-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



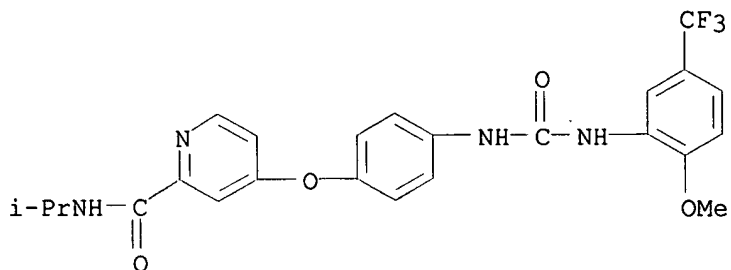
RN 284461-60-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



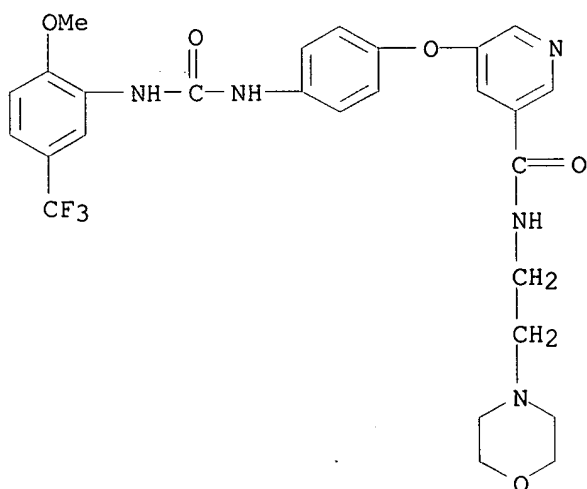
RN 284461-61-6 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



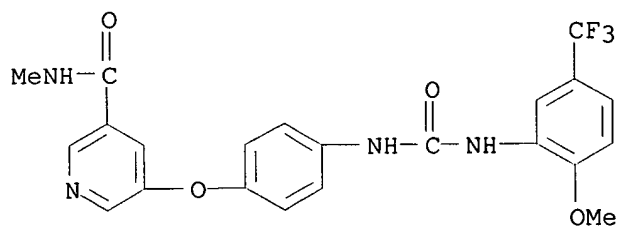
RN 284461-62-7 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



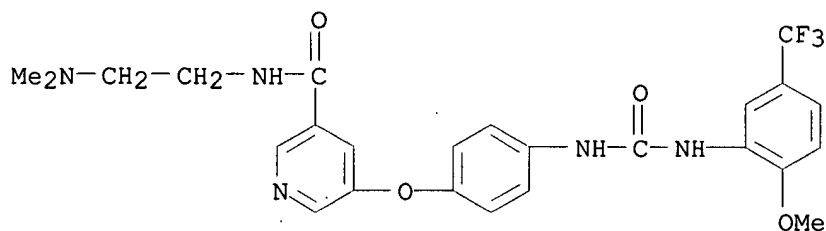
RN 284461-63-8 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



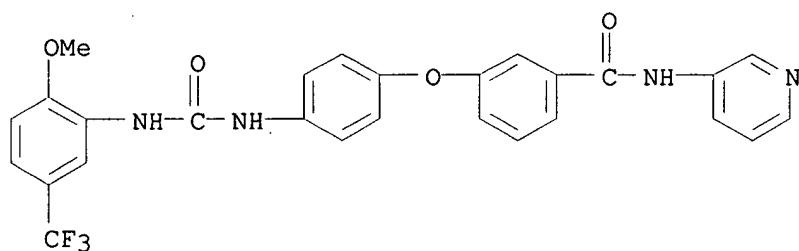
RN 284461-64-9 CAPLUS

CN 3-Pyridinecarboxamide, N-[2-(dimethylamino)ethyl]-5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



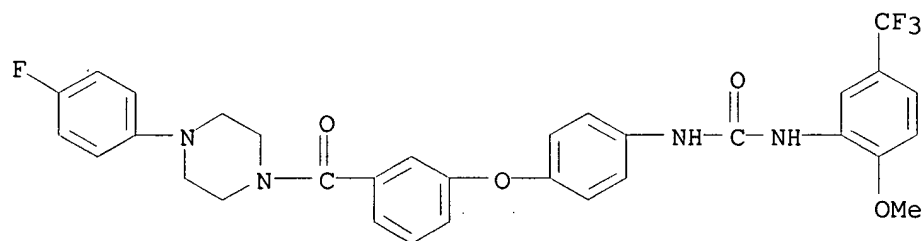
RN 284461-65-0 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-3-pyridinyl- (9CI) (CA INDEX NAME)



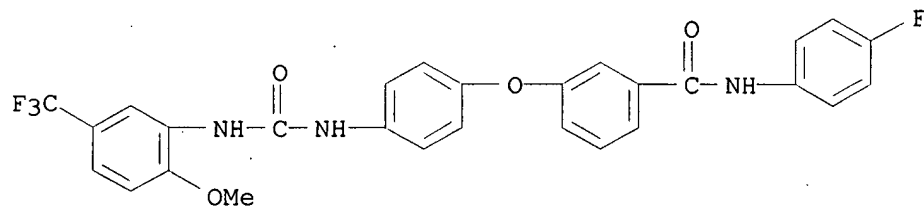
RN 284461-66-1 CAPLUS

CN Piperazine, 1-(4-fluorophenyl)-4-[3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]benzoyl]- (9CI) (CA INDEX NAME)



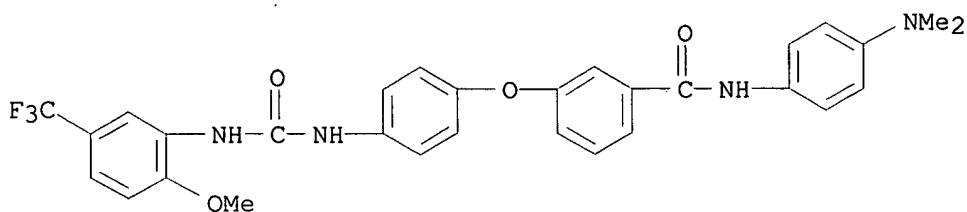
RN 284461-67-2 CAPLUS

CN Benzamide, N-(4-fluorophenyl)-3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



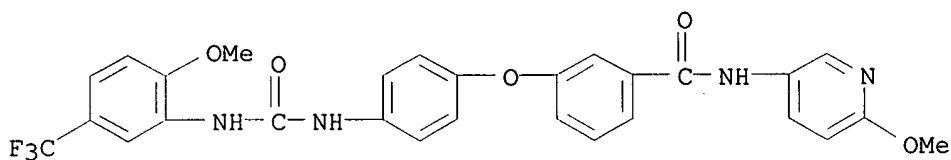
RN 284461-68-3 CAPLUS

CN Benzamide, N-[4-(dimethylamino)phenyl]-3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



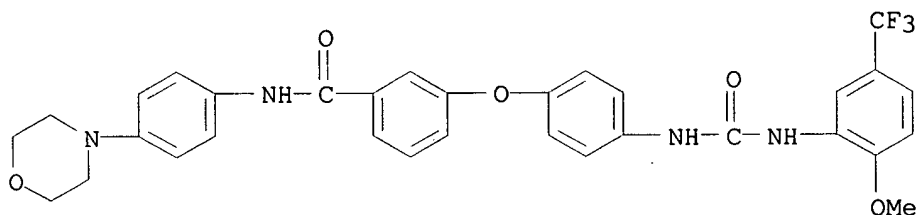
RN 284461-69-4 CAPLUS

CN Benzamide, N-(6-methoxy-3-pyridinyl)-3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



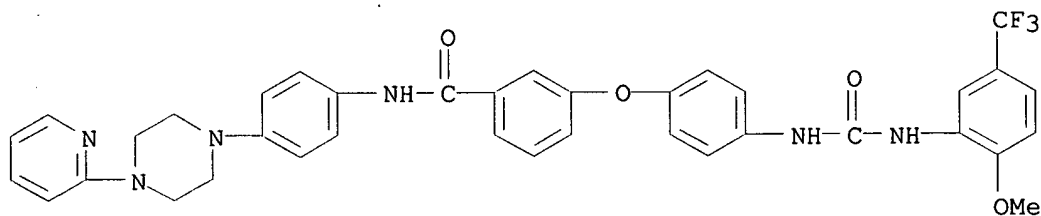
RN 284461-70-7 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



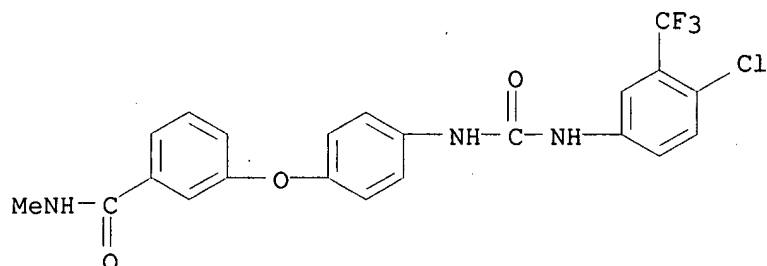
RN 284461-71-8 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-[4-(2-pyridinyl)-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



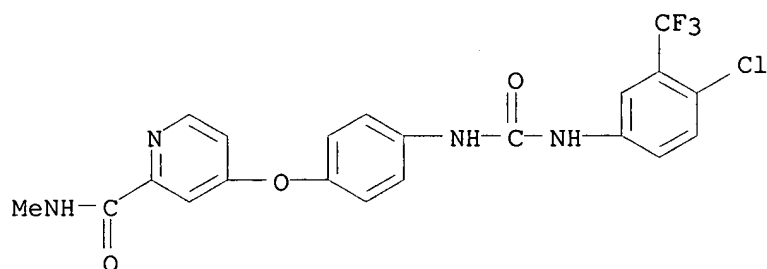
RN 284461-72-9 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



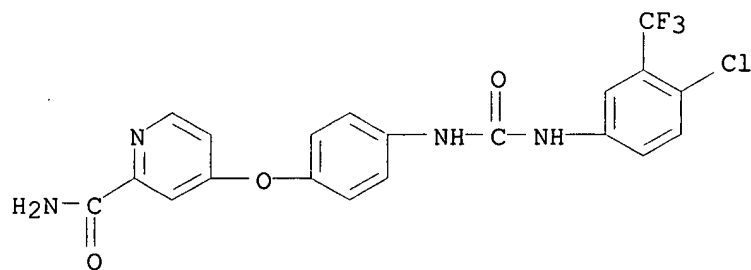
RN 284461-73-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



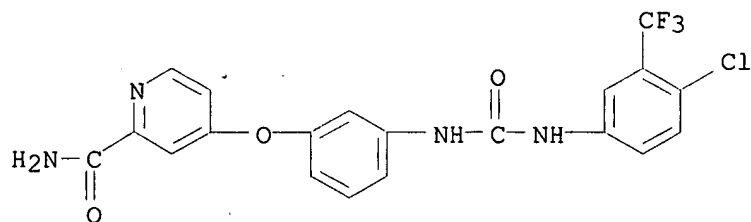
RN 284461-74-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



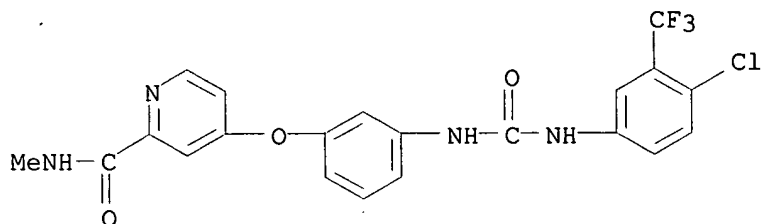
RN 284461-75-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



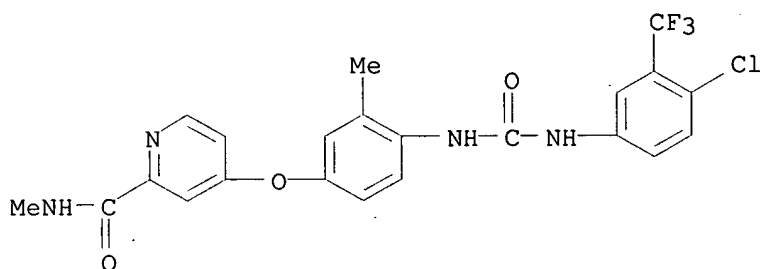
RN 284461-76-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



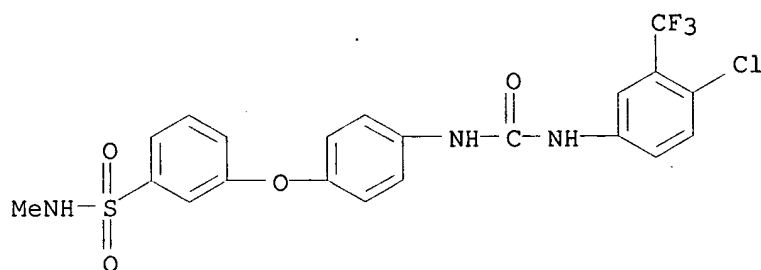
RN 284461-78-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-3-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-79-6 CAPLUS

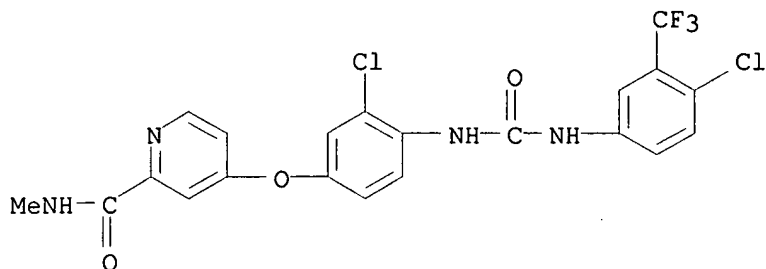
CN Benzenesulfonamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-80-9 CAPLUS

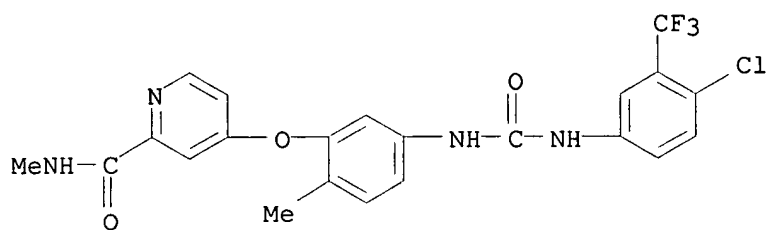
CN 2-Pyridinecarboxamide, 4-[3-chloro-4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)





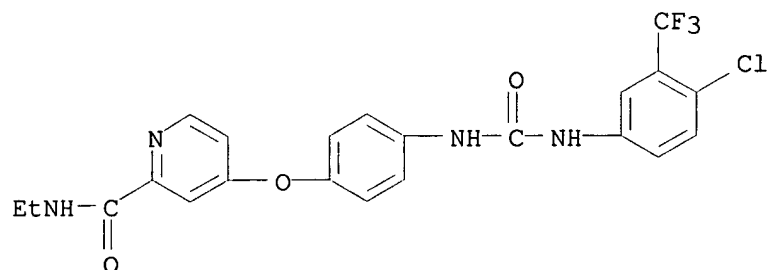
RN 284461-81-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



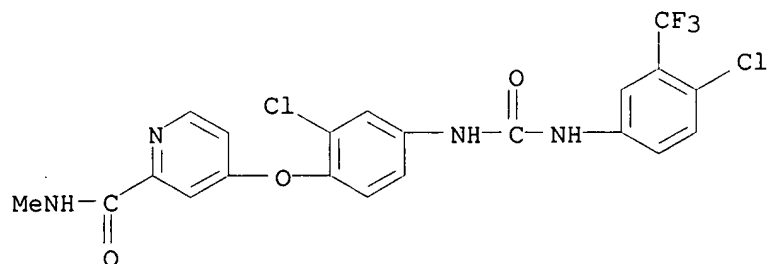
RN 284461-82-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-ethyl- (9CI) (CA INDEX NAME)

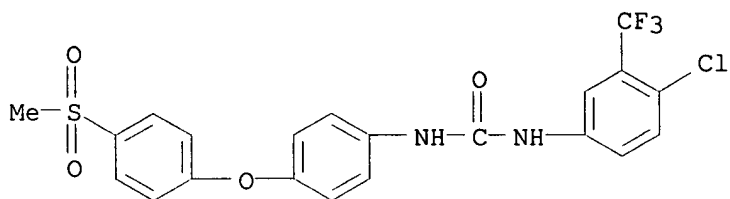


RN 284461-83-2 CAPLUS

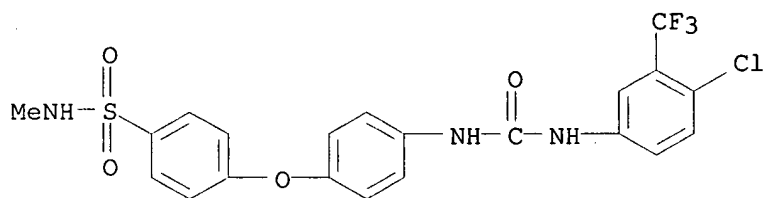
CN 2-Pyridinecarboxamide, 4-[2-chloro-4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



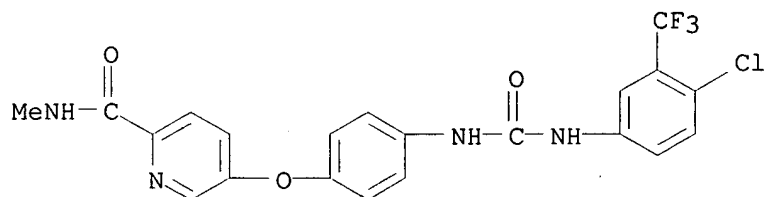
RN 284461-84-3 CAPLUS  
CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[4-(methylsulfonyl)phenoxy]phenyl]- (9CI) (CA INDEX NAME)



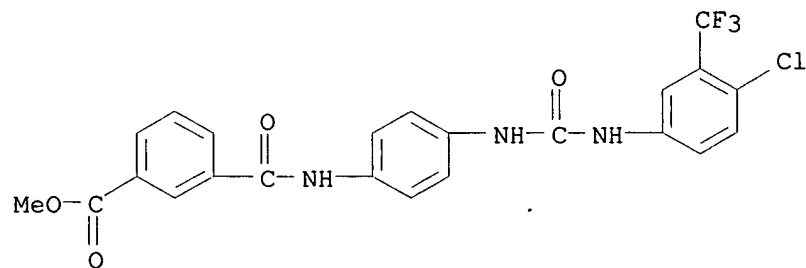
RN 284461-85-4 CAPLUS  
CN Benzenesulfonamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



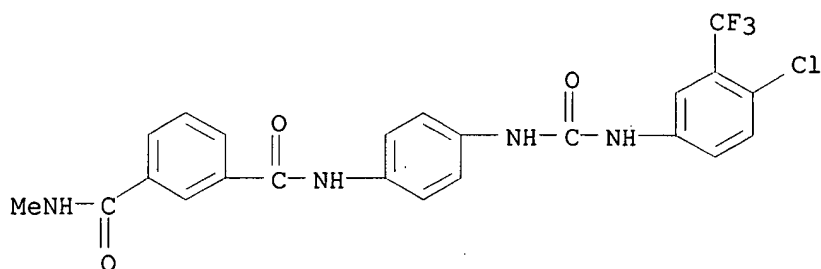
RN 284461-88-7 CAPLUS  
CN 2-Pyridinecarboxamide, 5-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-89-8 CAPLUS  
CN Benzoic acid, 3-[[[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

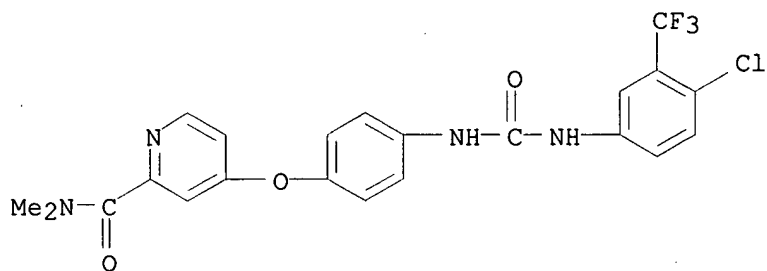


RN 284461-90-1 CAPLUS  
CN 1,3-Benzenedicarboxamide, N-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]-N'-methyl- (9CI) (CA INDEX NAME)



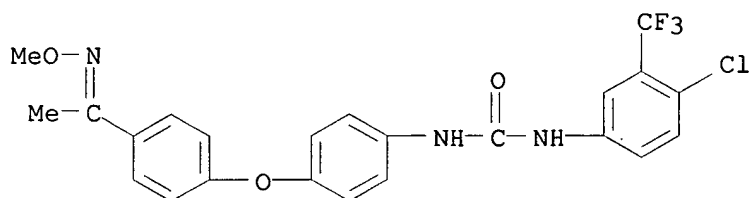
RN 284461-91-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



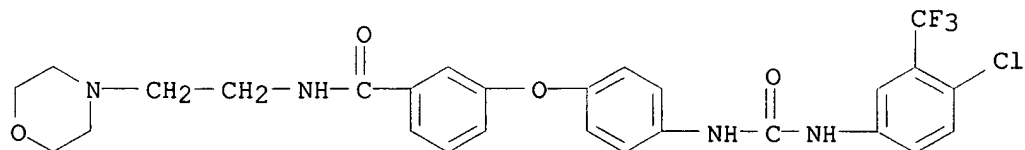
RN 284461-92-3 CAPLUS

CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[4-[1-(methoxyimino)ethyl]phenoxy]phenyl]- (9CI) (CA INDEX NAME)



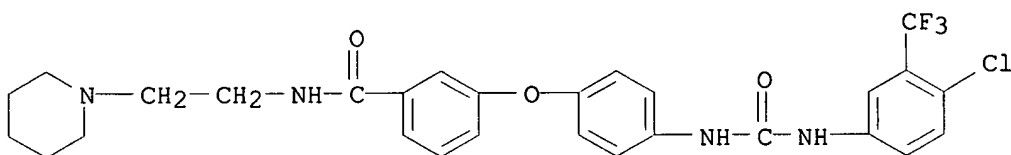
RN 284461-93-4 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



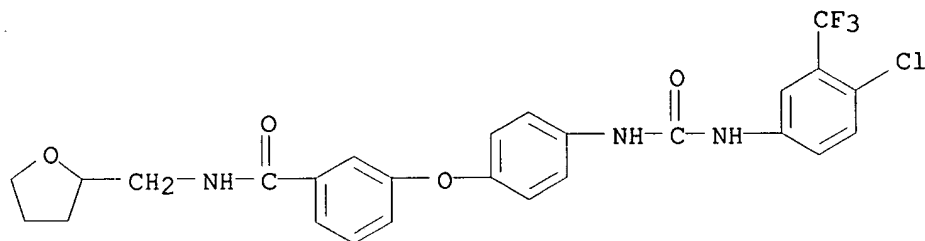
RN 284461-94-5 CAPLUS

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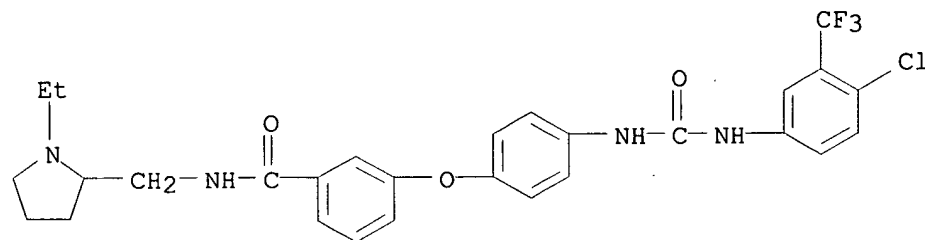
RN 284461-95-6 CAPLUS

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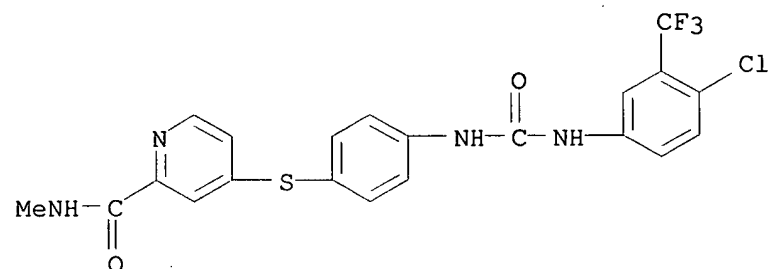
RN 284461-96-7 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[(1-ethyl-2-pyrrolidinyl)methyl]- (9CI) (CA INDEX NAME)



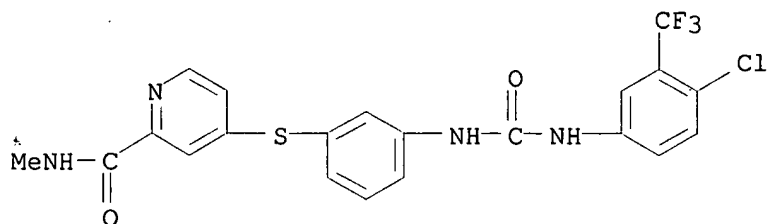
RN 284461-97-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



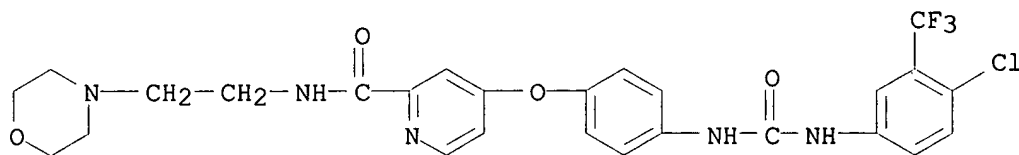
RN 284462-01-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



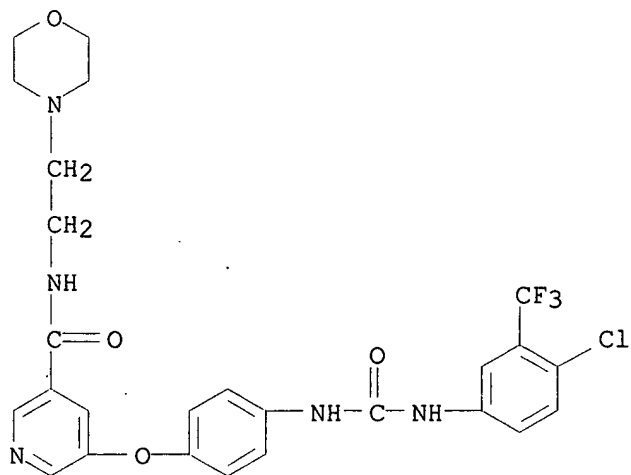
RN 284462-02-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



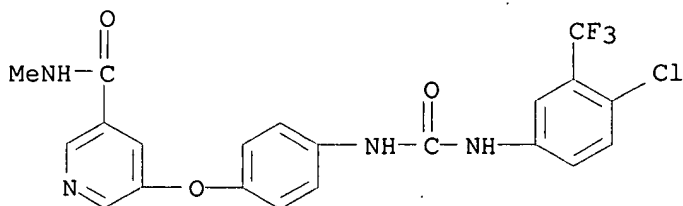
RN 284462-03-9 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



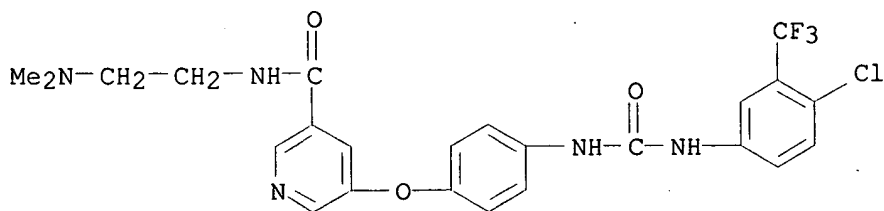
RN 284462-04-0 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



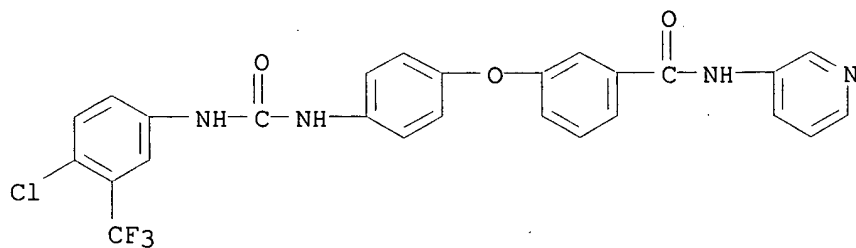
RN 284462-05-1 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



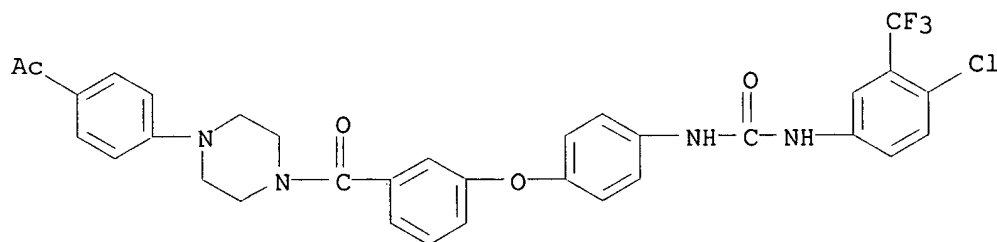
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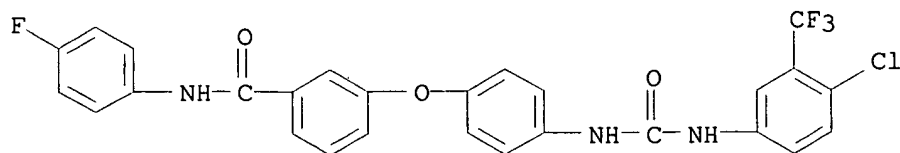
RN 284462-08-4 CAPLUS

CN Piperazine, 1-(4-acetylphenyl)-4-[3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]benzoyl]- (9CI) (CA INDEX NAME)



RN 284462-09-5 CAPLUS

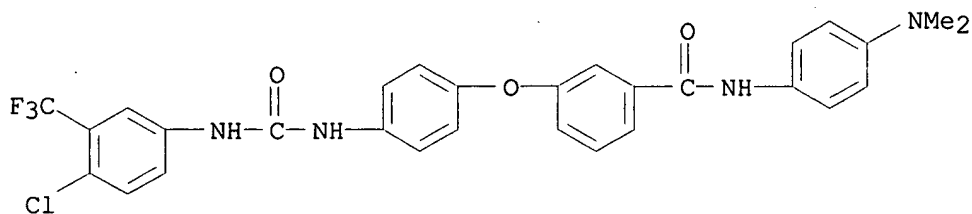
CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 284462-10-8 CAPLUS

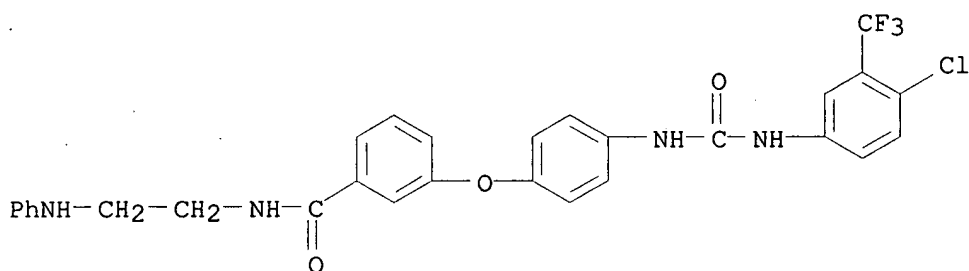
CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(4-fluorophenyl)- (9CI) (CA INDEX NAME)

o]phenoxy]-N-[4-(dimethylamino)phenyl]- (9CI) (CA INDEX NAME)



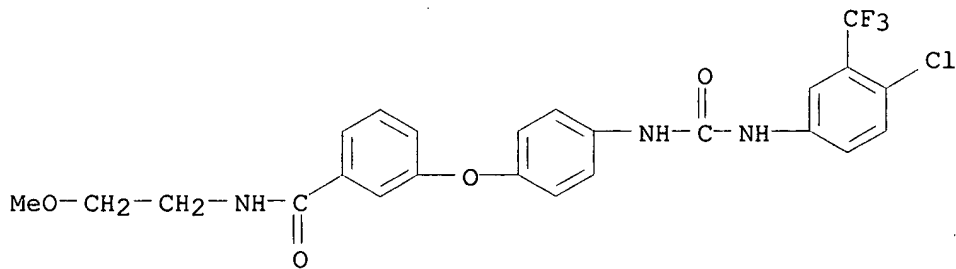
RN 284462-11-9 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(phenylamino)ethyl]- (9CI) (CA INDEX NAME)



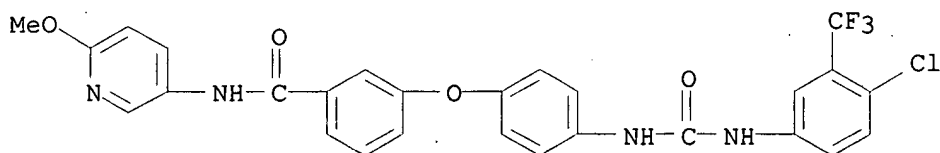
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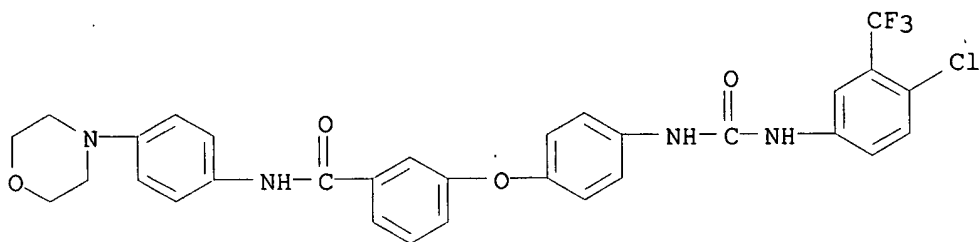
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CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(6-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



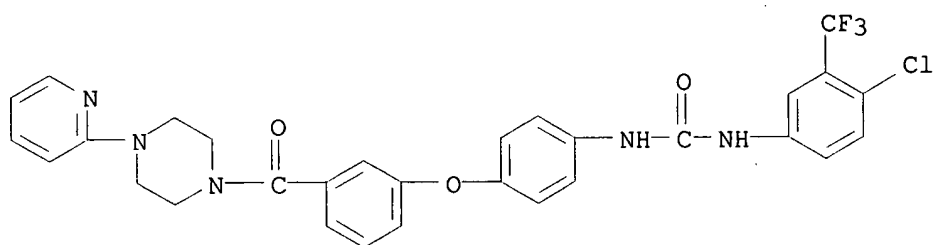
RN 284462-15-3 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



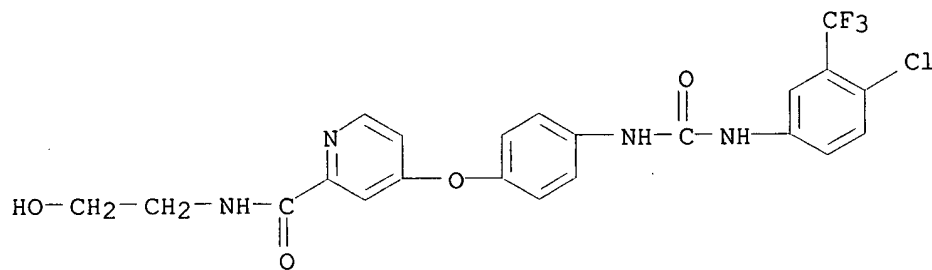
RN 284462-16-4 CAPLUS

CN Piperazine, 1-[3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]benzoyl]-4-(2-pyridinyl)- (9CI) (CA INDEX NAME)



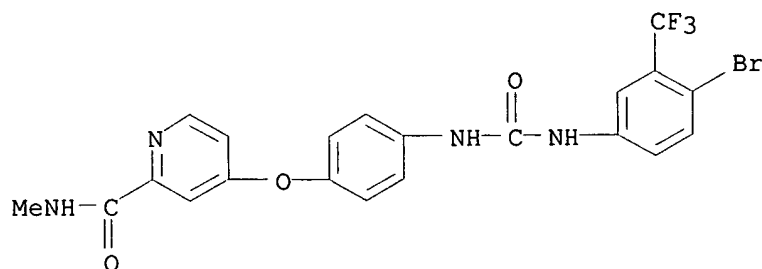
RN 284462-17-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



RN 284462-18-6 CAPLUS

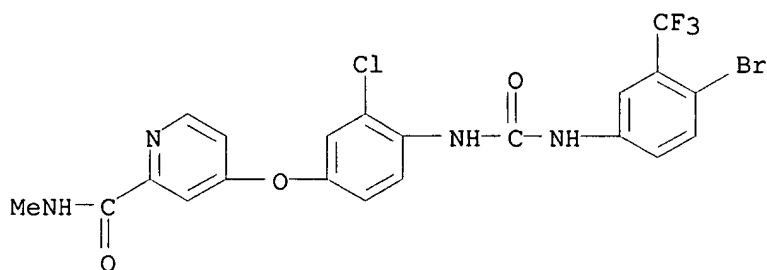
CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)





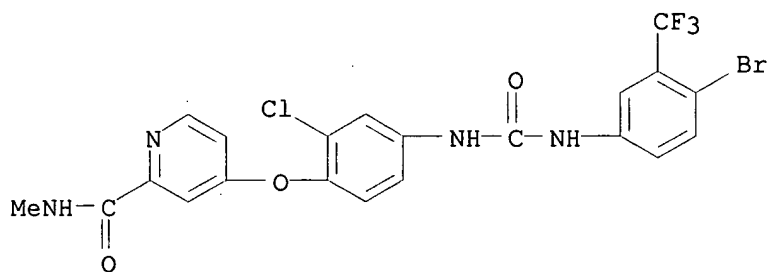
RN 284462-19-7 CAPLUS

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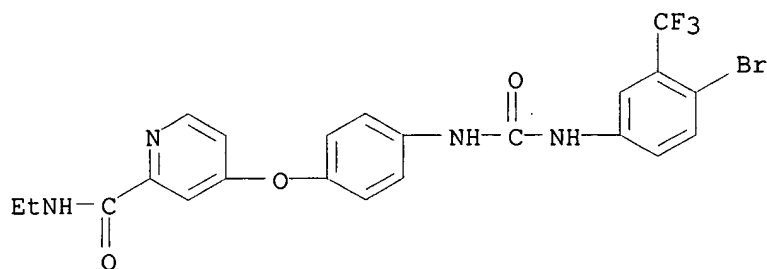
RN 284462-20-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonylamino]-2-chlorophenoxy]-N-methyl- (9CI) (CA INDEX NAME)



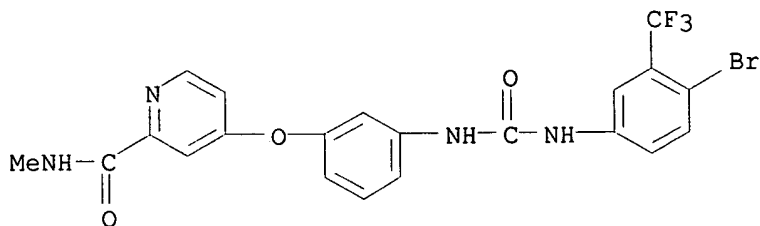
RN 284462-21-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonylamino]phenoxy]-N-ethyl- (9CI) (CA INDEX NAME)



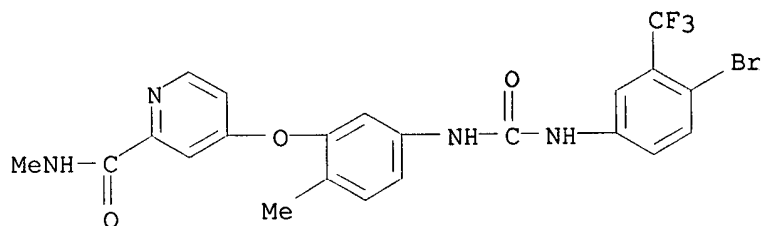
RN 284462-22-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonylamino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



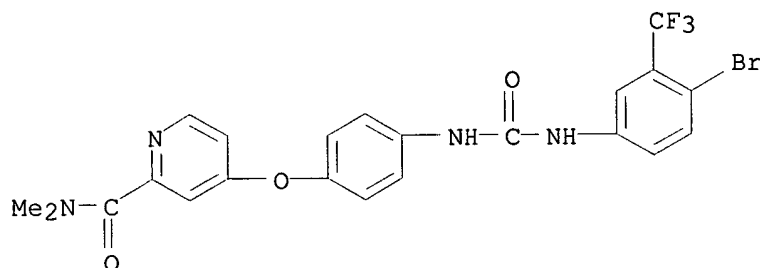
RN 284462-23-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



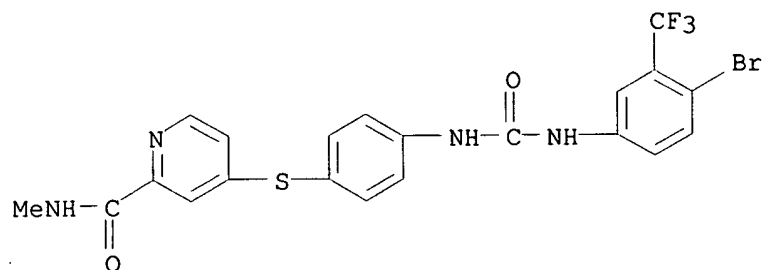
RN 284462-24-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



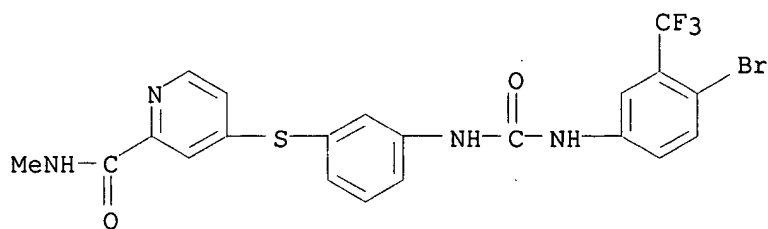
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CN 2-Pyridinecarboxamide, 4-[[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



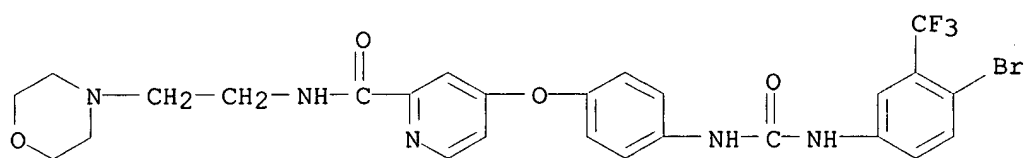
RN 284462-26-6 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



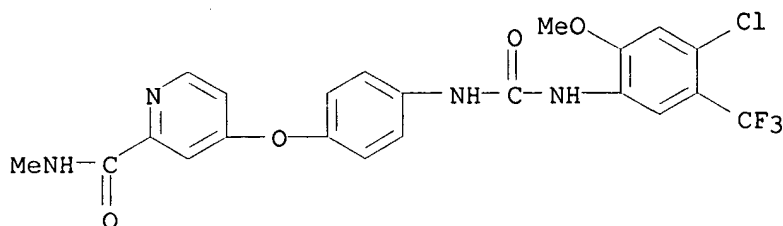
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CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



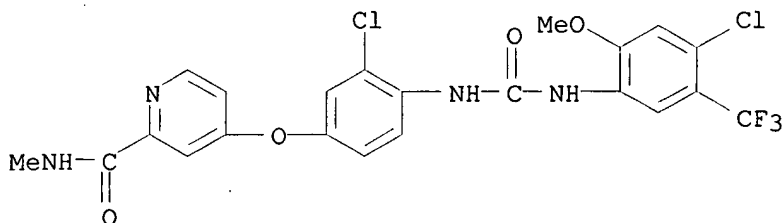
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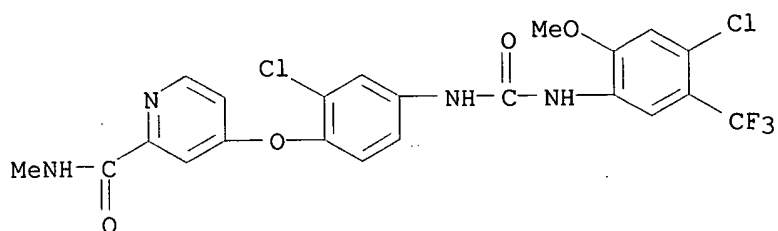
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CN 2-Pyridinecarboxamide, 4-[3-chloro-4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



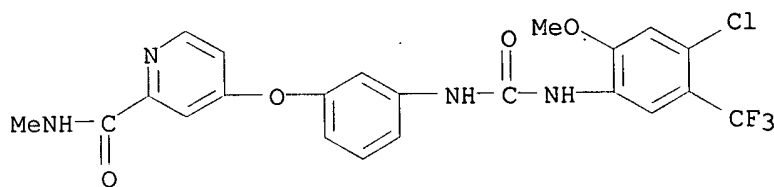
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CN 2-Pyridinecarboxamide, 4-[2-chloro-4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



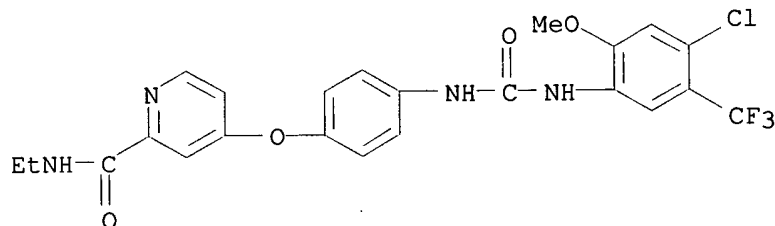
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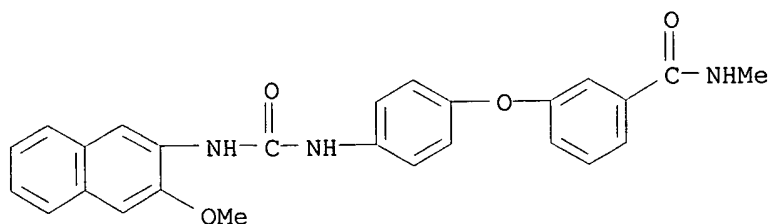
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CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-ethyl- (9CI) (CA INDEX NAME)



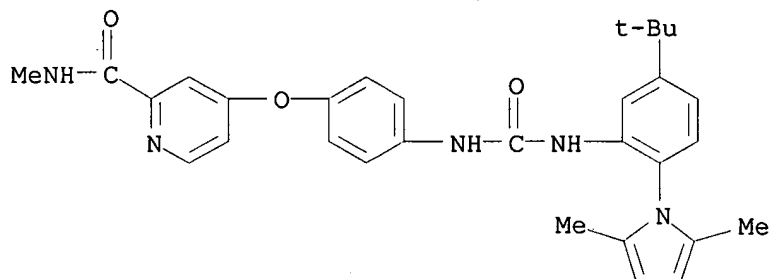
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CN Benzamide, 3-[4-[[[3-methoxy-2-naphthalenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

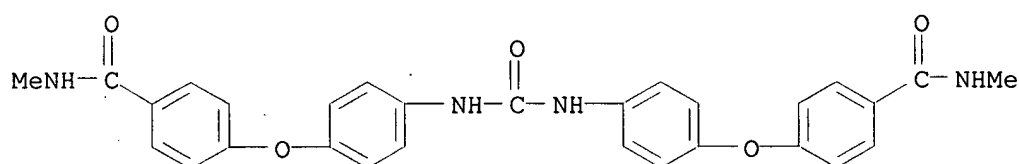


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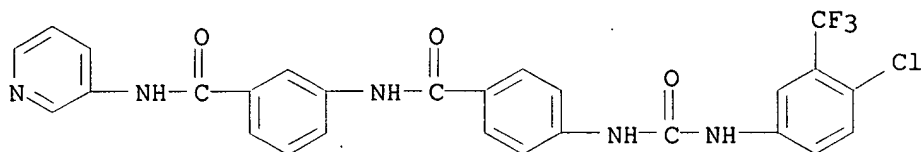
CN 2-Pyridinecarboxamide, 4-[4-[[[5-(1,1-dimethylethyl)-2-(2,5-dimethyl-1H-pyrrol-1-yl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



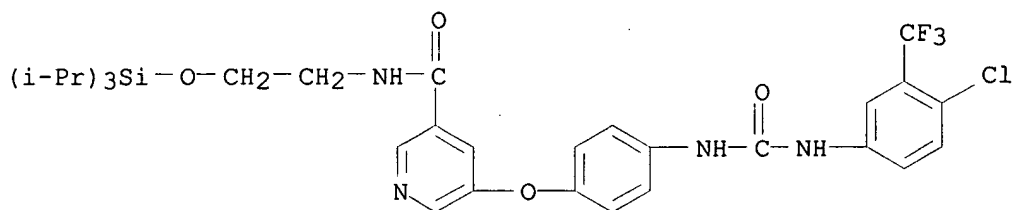
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 (CA INDEX NAME)



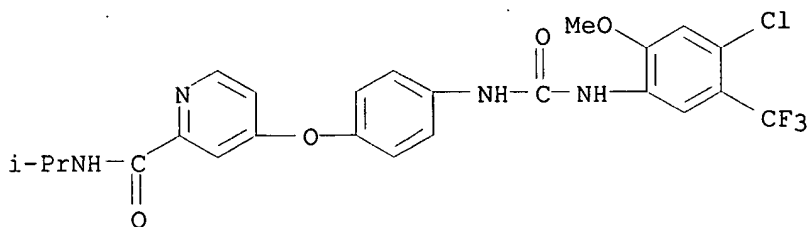
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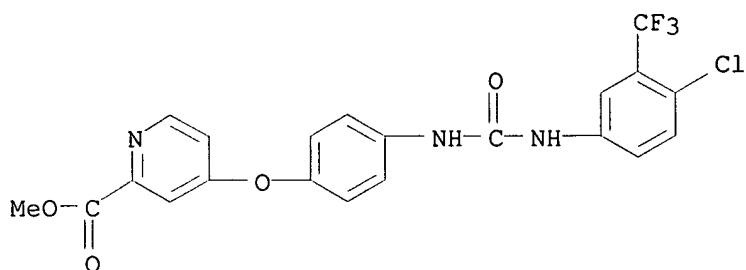
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 (CA INDEX NAME)



RN 447457-09-2 CAPLUS  
 CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

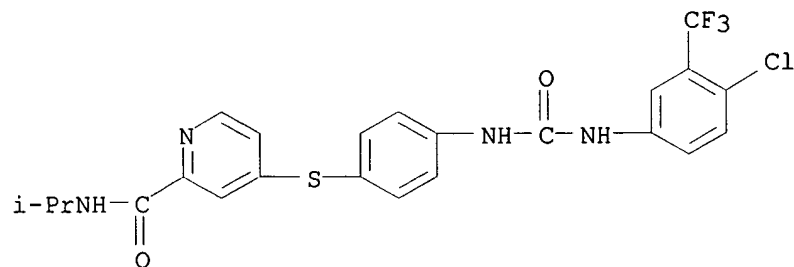


RN 573673-43-5 CAPLUS

CN 2-Pyridinecarboxylic acid, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
(CA INDEX NAME)

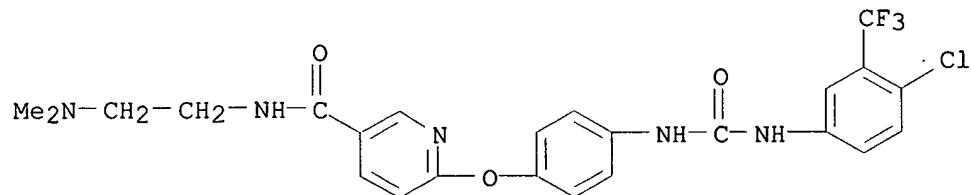
RN 604813-02-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 604813-04-9 CAPLUS

CN 3-Pyridinecarboxamide, 6-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)

L122 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2003:590832 CAPLUS

Searched by Barb O'Bryen, STIC 571-272-2518

DOCUMENT NUMBER: 139:149528  
TITLE: Preparation of diphenylureas as RAF kinase inhibitors  
INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.  
PATENT ASSIGNEE(S): Bayer Corporation, USA  
SOURCE: U.S. Pat. Appl. Publ., 62 pp., Cont. of U. S. Ser. No. 42,203  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003144278	A1	20030731	US 2002-283248	20021030
PRIORITY APPLN. INFO.:			US 2001-367380P P	20010112
			US 2002-42203 A1	20020111

OTHER SOURCE(S): MARPAT 139:149528

ED Entered STN: 01 Aug 2003

AB ADB [I; D = NHCONH; A = L(ML1)q; L = 5-6 membered cyclic structure bound directly to D; L1 = substituted cyclic moiety having .gtoreq.5 members, M = bridging group having .gtoreq.1 atom; q = 1-3; L, L1 contain 0-4 N, O, S; B = (substituted) up to tricyclic aryl, heteroaryl of .ltoreq.30 C atoms with .gtoreq.1 6-membered cyclic structure bound directly to D contg. 0-4 N, O, S], were prepd. Thus, 4-chloro-3-(trifluoromethyl)phenyl isocyanate in CH2Cl2 was added dropwise to a suspension of 4-[2-(N-methylcarbamoyl)-4-pyridyloxy]aniline (prepn. given) in CH2Cl2 at 0.degree.; the resulting mixt. was stirred at room temp. for 22 h. to afford N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea. I inhibited RAF kinase in the range 1 nM-1 .mu.M. I pharmaceutical compns. are claimed.

IT 139691-76-2, Raf kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; prepn. of diphenylureas as RAF kinase inhibitors)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

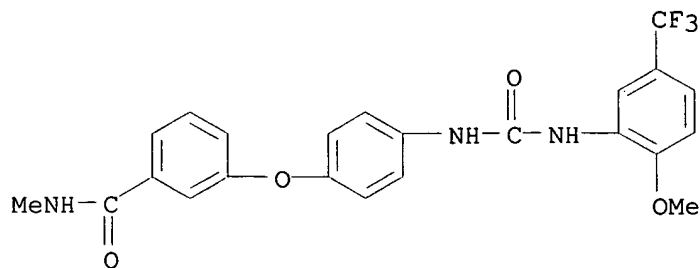
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284461-65-0P 284461-66-1P 284461-67-2P  
284461-68-3P 284461-69-4P 284461-70-7P  
284461-71-8P 284461-72-9P 284461-73-0P,  
N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl]urea 284461-75-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl] urea 284461-76-3P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284461-78-5P 284461-80-9P  
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284461-95-6P 284461-96-7P 284461-97-8P  
284461-98-9P 284461-99-0P 284462-01-7P  
284462-02-8P 284462-03-9P 284462-04-0P  
284462-05-1P 284462-07-3P 284462-08-4P  
284462-09-5P 284462-10-8P 284462-11-9P  
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284462-16-4P 284462-17-5P 284462-18-6P,  
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447457-09-2P 474642-55-2P 573673-42-4P  
573673-43-5P 573673-45-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

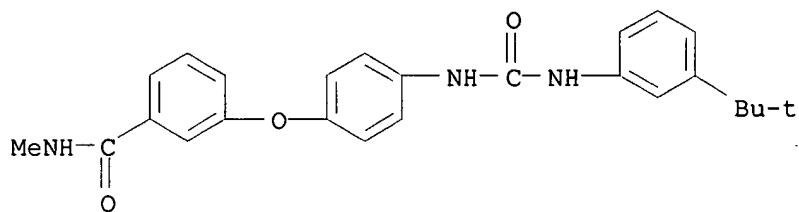
(prepn. of diphenylureas as RAF kinase inhibitors)

RN 228418-48-2 CAPLUS  
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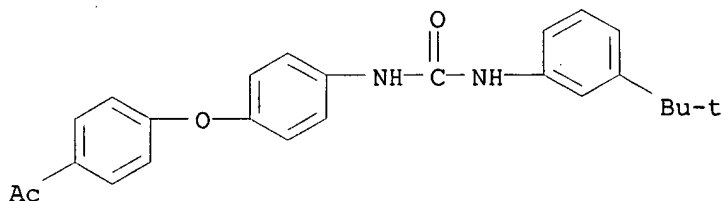
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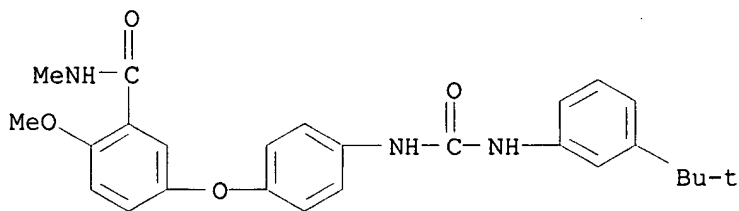
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(9CI) (CA INDEX NAME)



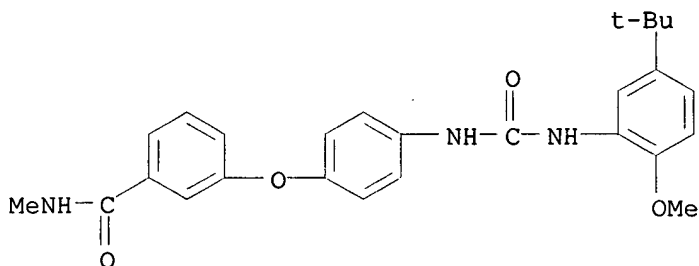
RN 284461-35-4 CAPLUS

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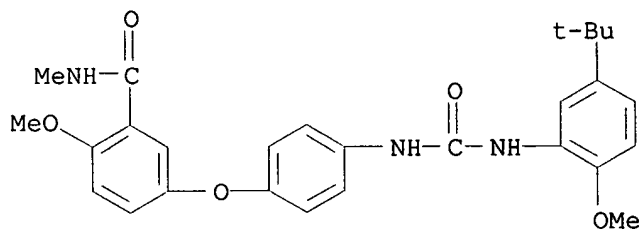
RN 284461-36-5 CAPLUS

CN Benzamide, 3-[4-[[[5-(1,1-dimethylethyl)-2-methoxyphenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



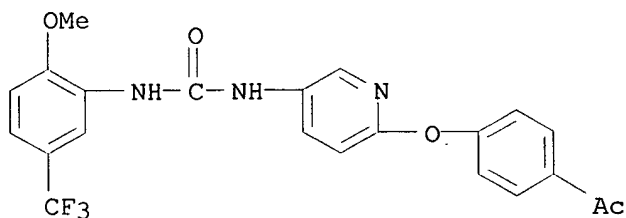
RN 284461-37-6 CAPLUS

CN Benzamide, 5-[4-[[[5-(1,1-dimethylethyl)-2-methoxyphenyl]amino]carbonyl]amino]phenoxy]-2-methoxy-N-methyl- (9CI) (CA INDEX NAME)



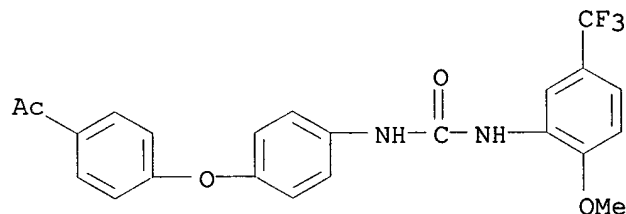
RN 284461-40-1 CAPLUS

CN Urea, N-[6-(4-acetylphenoxy)-3-pyridinyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



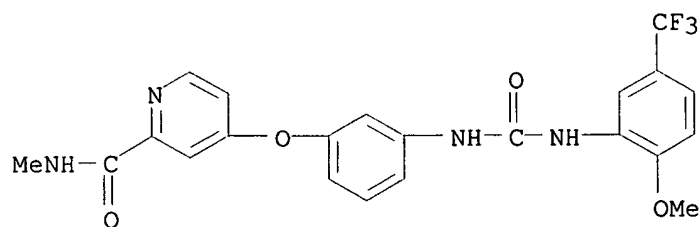
RN 284461-41-2 CAPLUS

CN Urea, N-[4-(4-acetylphenoxy)phenyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



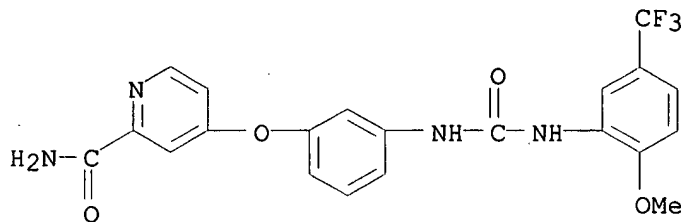
RN 284461-42-3 CAPLUS

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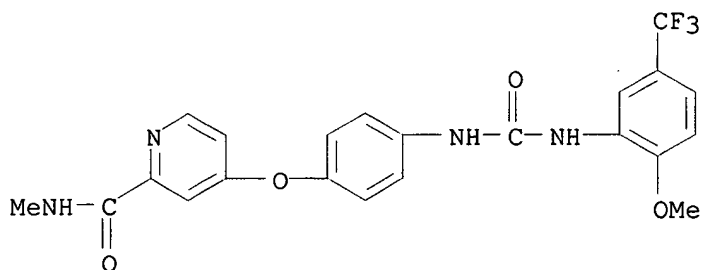
RN 284461-43-4 CAPLUS

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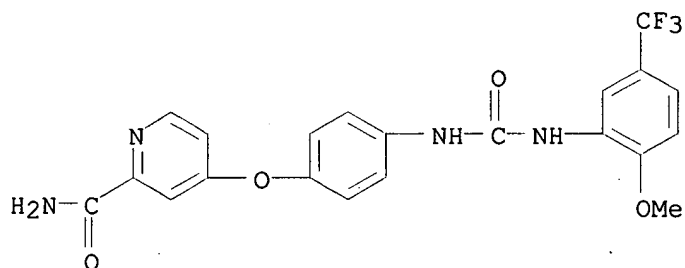
RN 284461-44-5 CAPLUS

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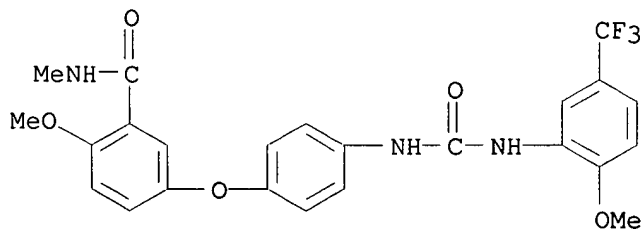
RN 284461-45-6 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



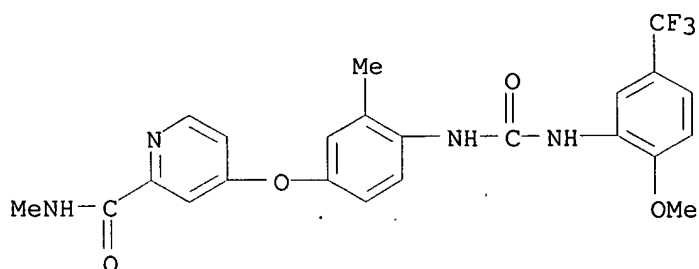
RN 284461-46-7 CAPLUS

CN Benzamide, 2-methoxy-5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



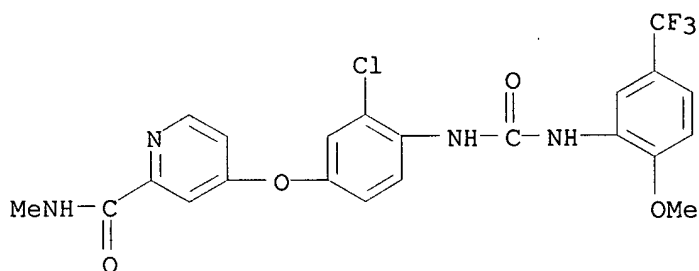
RN 284461-47-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]-3-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



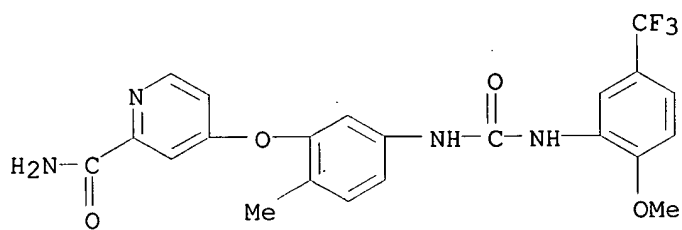
RN 284461-48-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-chloro-4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



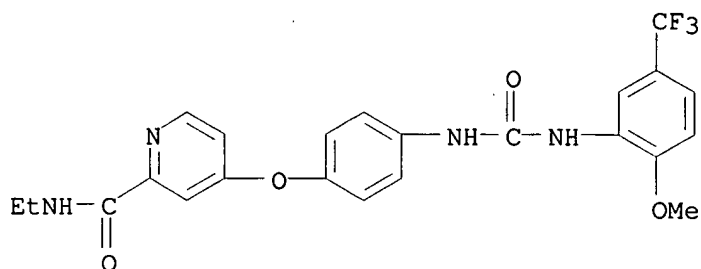
RN 284461-49-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]- (9CI) (CA INDEX NAME)



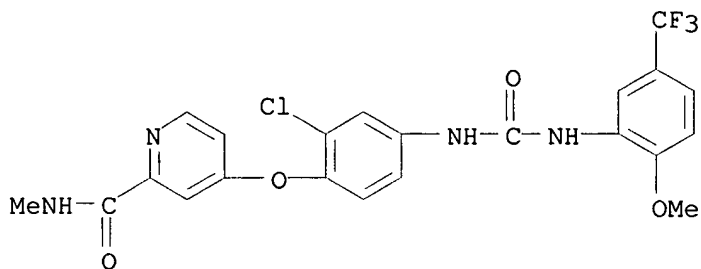
RN 284461-50-3 CAPLUS

CN 2-Pyridinecarboxamide, N-ethyl-4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



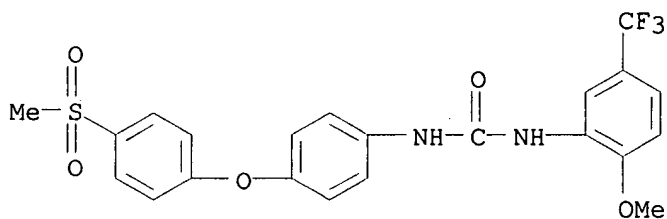
RN 284461-51-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[2-chloro-4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



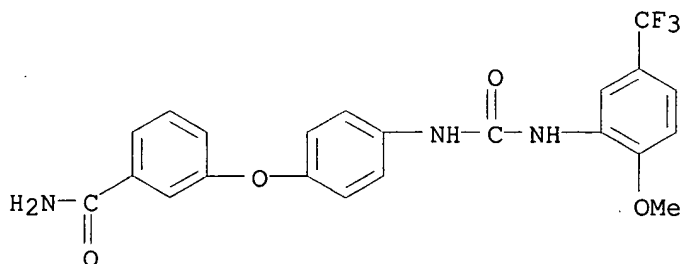
RN 284461-52-5 CAPLUS

CN Urea, N-[2-methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[4-(methylsulfonyl)phenoxy]phenyl]- (9CI) (CA INDEX NAME)



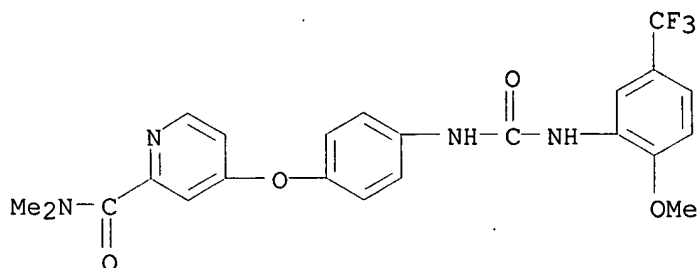
RN 284461-53-6 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



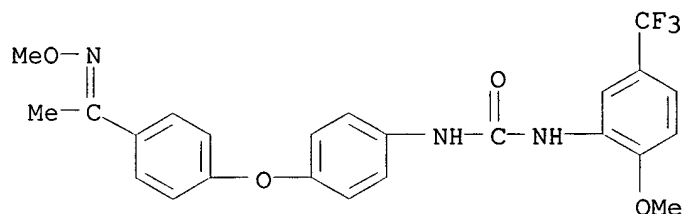
RN 284461-55-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



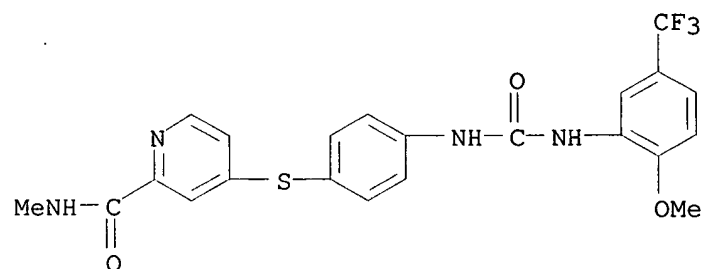
RN 284461-57-0 CAPLUS

CN Urea, N-[4-[4-[1-(methoxyimino)ethyl]phenoxy]phenyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



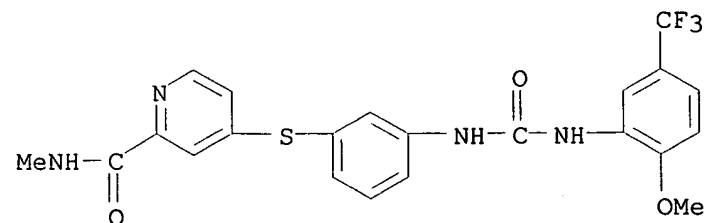
RN 284461-58-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



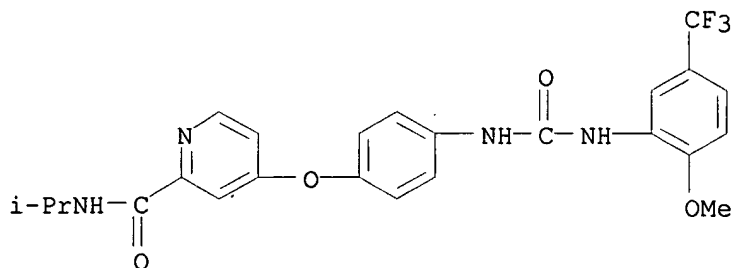
RN 284461-60-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



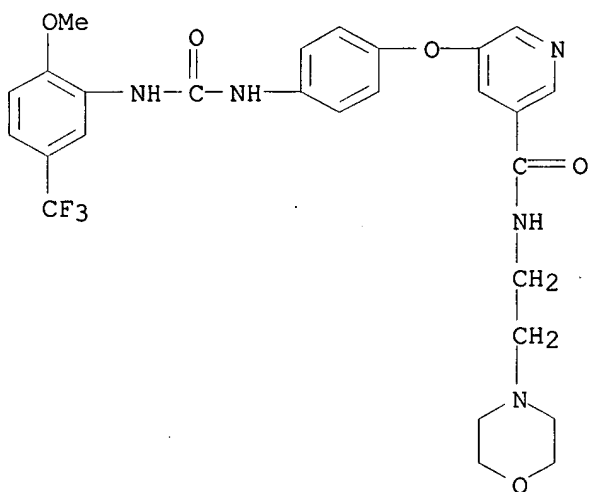
RN 284461-61-6 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



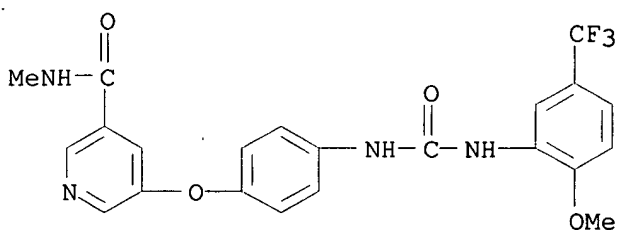
RN 284461-62-7 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



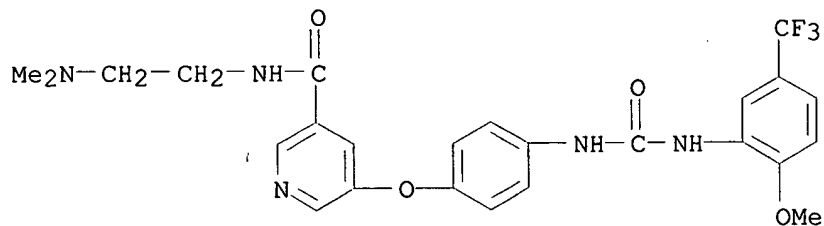
RN 284461-63-8 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



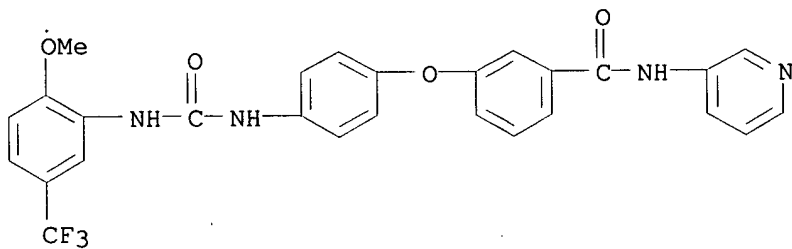
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CN 3-Pyridinecarboxamide, N-[2-(dimethylamino)ethyl]-5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



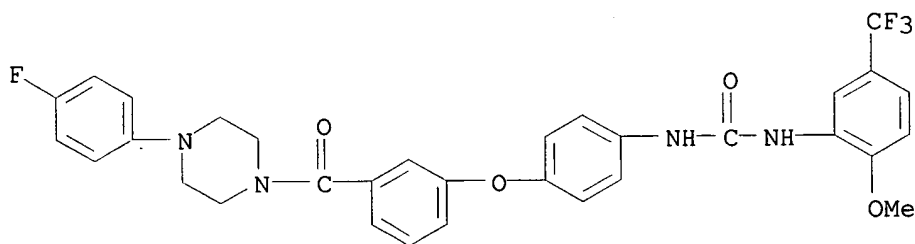
RN 284461-65-0 CAPLUS

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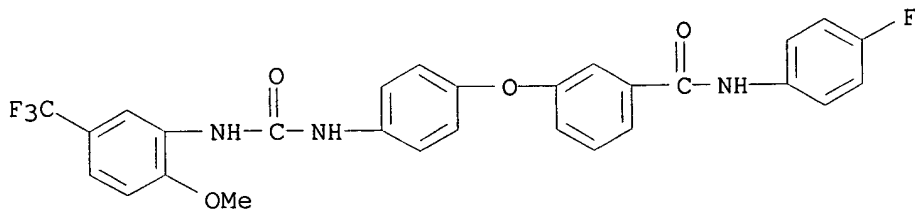
RN 284461-66-1 CAPLUS

CN Piperazine, 1-(4-fluorophenyl)-4-[3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]benzoyl]- (9CI) (CA INDEX NAME)



RN 284461-67-2 CAPLUS

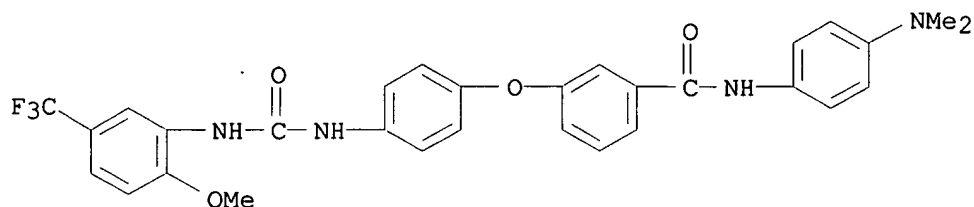
CN Benzamide, N-(4-fluorophenyl)-3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



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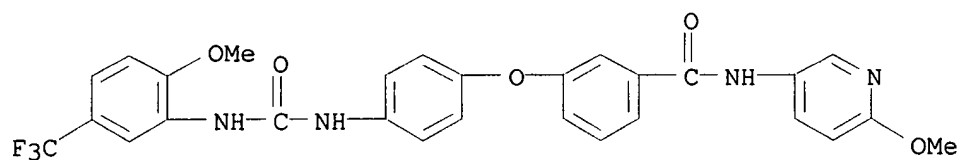
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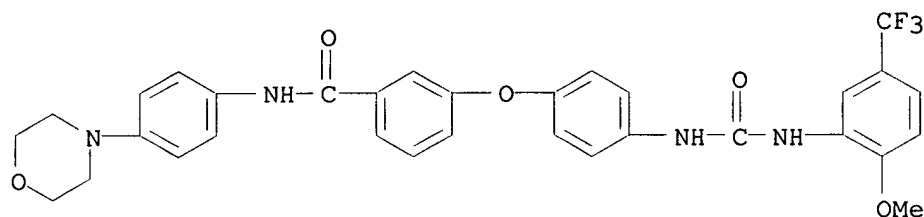
RN 284461-69-4 CAPLUS

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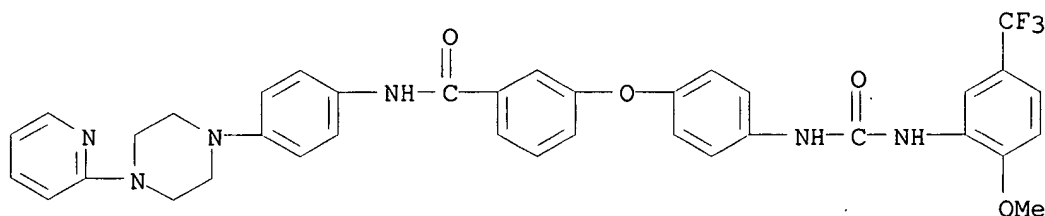
RN 284461-70-7 CAPLUS

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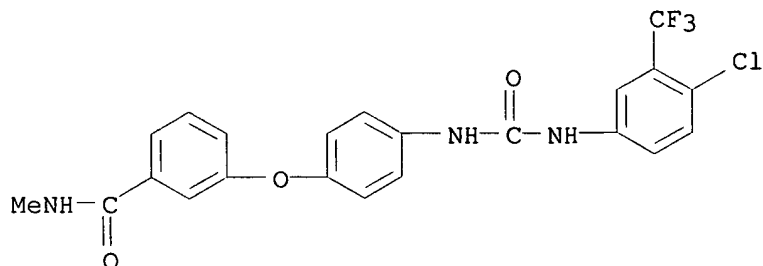
RN 284461-71-8 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-[4-(2-pyridinyl)-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



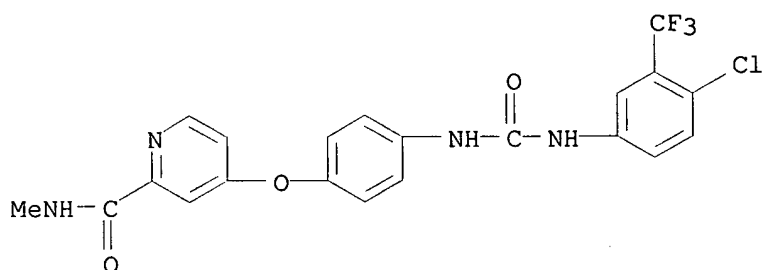
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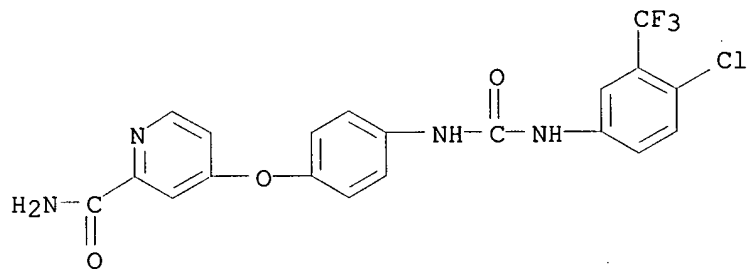
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CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



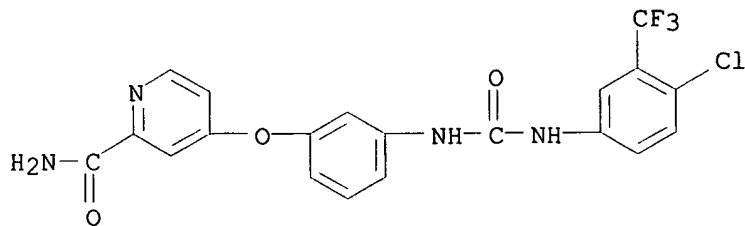
RN 284461-74-1 CAPLUS

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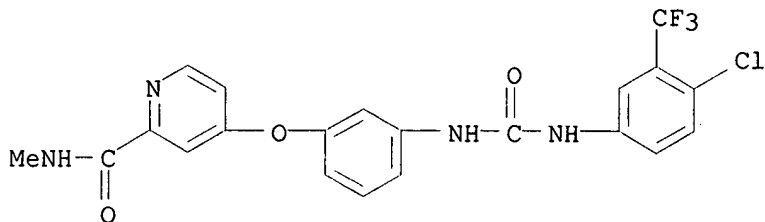
RN 284461-75-2 CAPLUS

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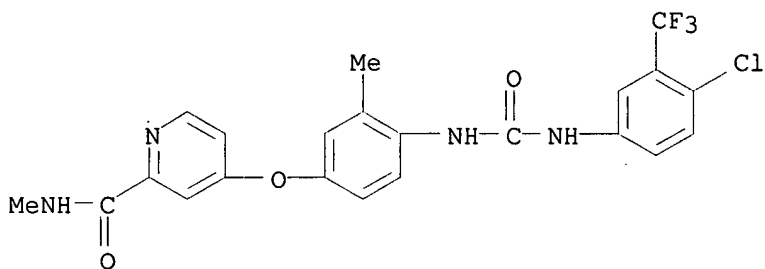
RN 284461-76-3 CAPLUS

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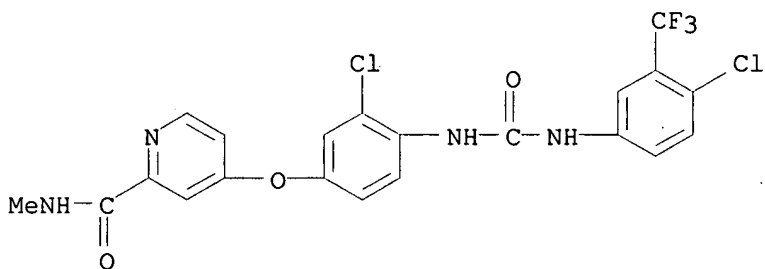
RN 284461-78-5 CAPLUS

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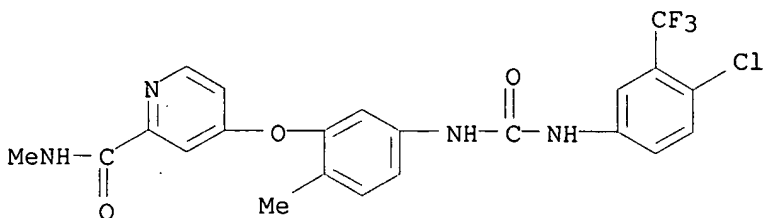
RN 284461-80-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-chloro-4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



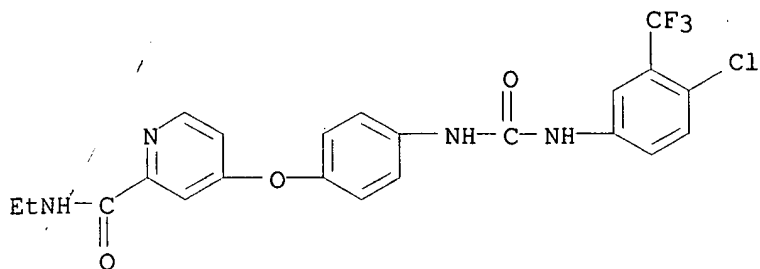
RN 284461-81-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



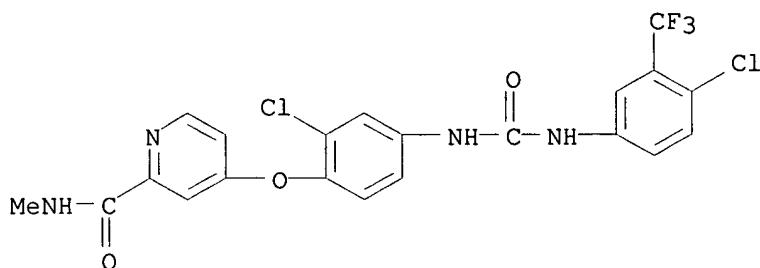
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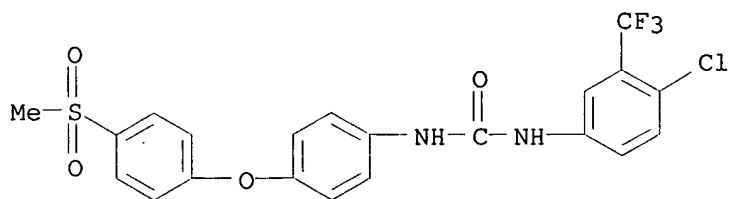
RN 284461-83-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[2-chloro-4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



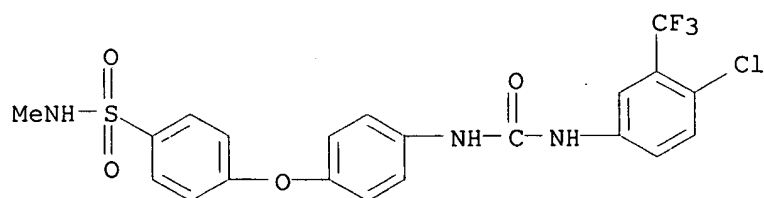
RN 284461-84-3 CAPLUS

CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[4-(methylsulfonyl)phenoxy]phenyl]- (9CI) (CA INDEX NAME)



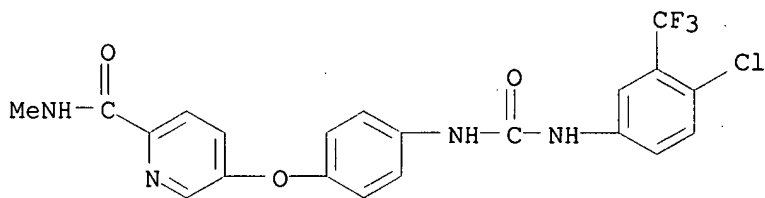
RN 284461-85-4 CAPLUS

CN Benzenesulfonamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



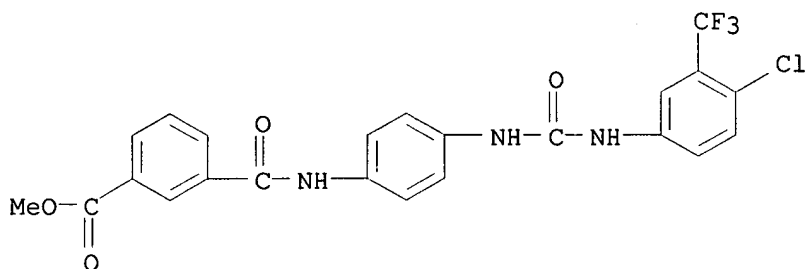
RN 284461-88-7 CAPLUS

CN 2-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



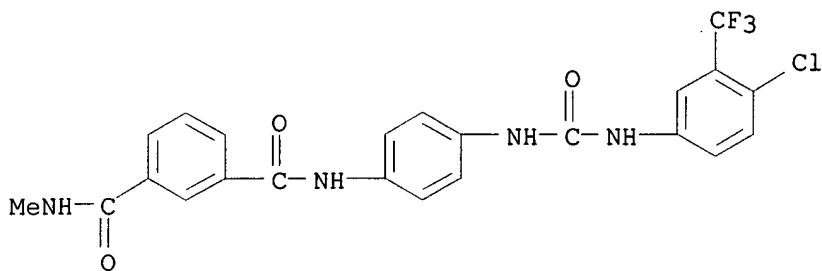
RN 284461-89-8 CAPLUS

CN Benzoic acid, 3-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



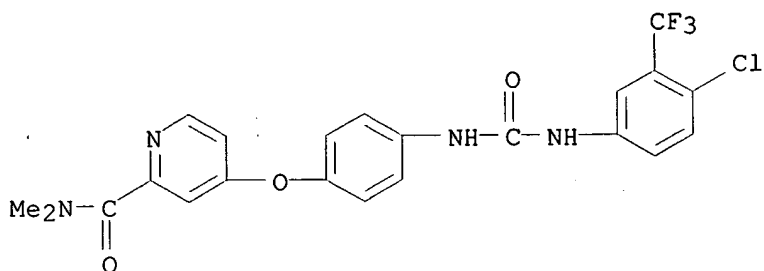
RN 284461-90-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]-N'-methyl- (9CI) (CA INDEX NAME)



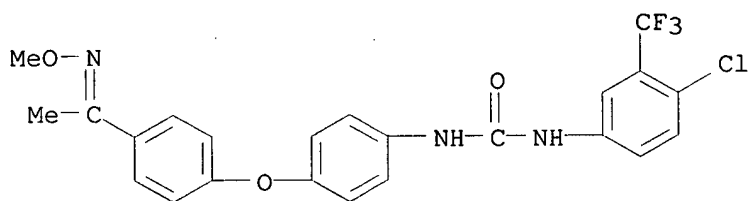
RN 284461-91-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



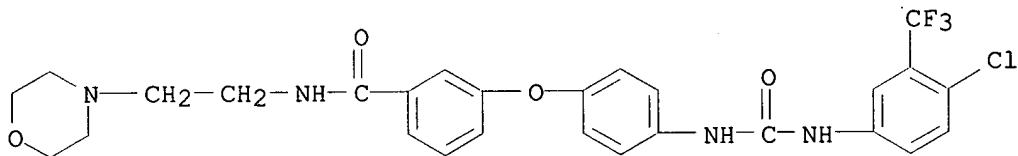
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CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[4-[1-(methoxyimino)ethyl]phenoxy]phenyl]- (9CI) (CA INDEX NAME)



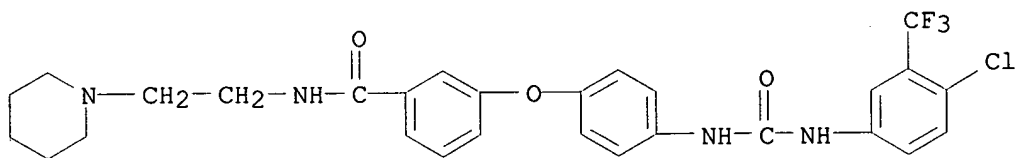
RN 284461-93-4 CAPLUS

CN Benzamide, 3-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



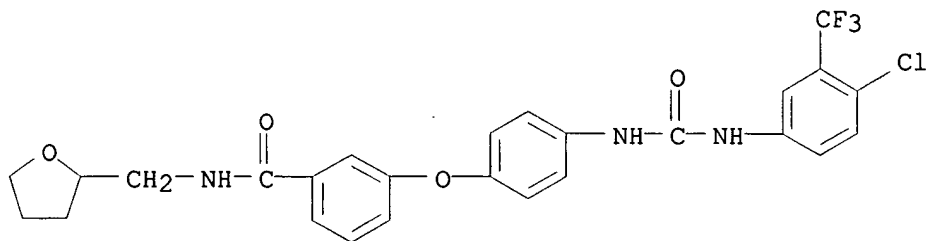
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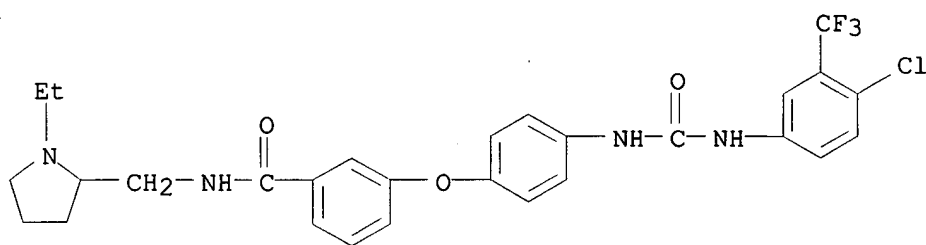
RN 284461-95-6 CAPLUS

CN Benzamide, 3-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



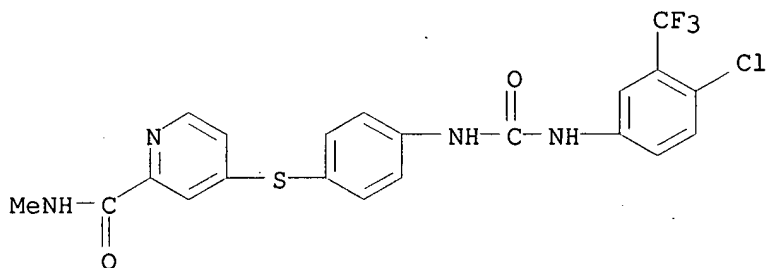
RN 284461-96-7 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl 1-ethyl-2-pyrrolidinylmethylether- (9CI) (CA INDEX NAME)



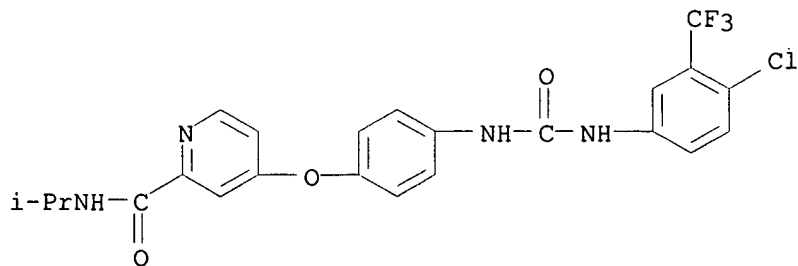
RN 284461-97-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



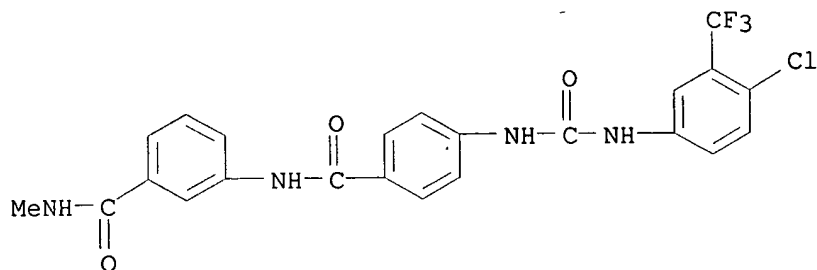
RN 284461-98-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



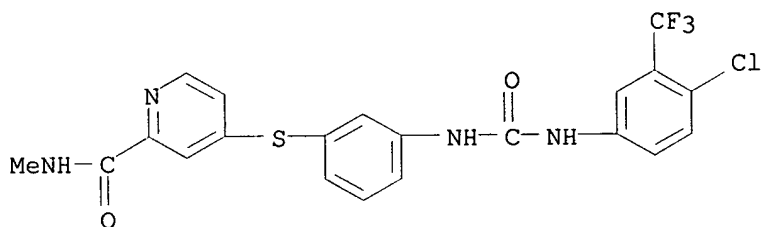
RN 284461-99-0 CAPLUS

CN Benzamide, 3-[[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]benzoyl]amino]-N-methyl- (9CI) (CA INDEX NAME)



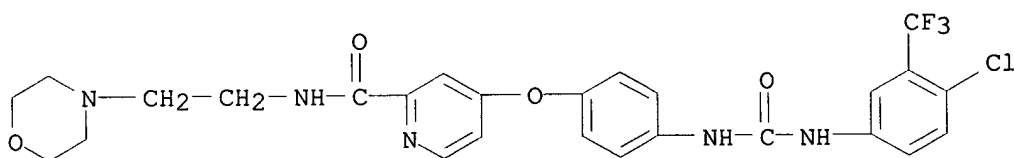
RN 284462-01-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[3-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-02-8 CAPLUS

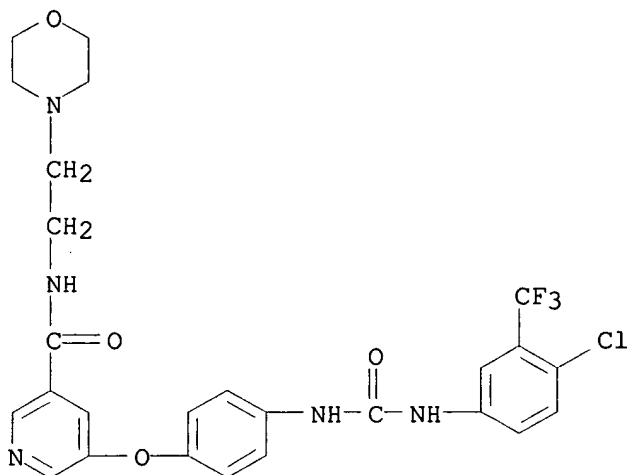
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 284462-03-9 CAPLUS

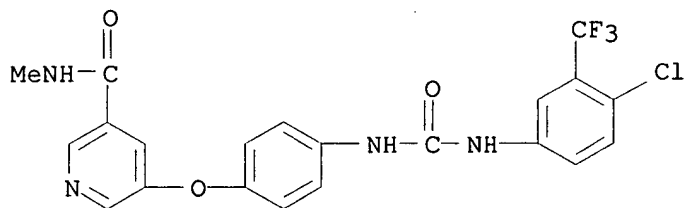
CN 3-Pyridinecarboxamide, 5-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)





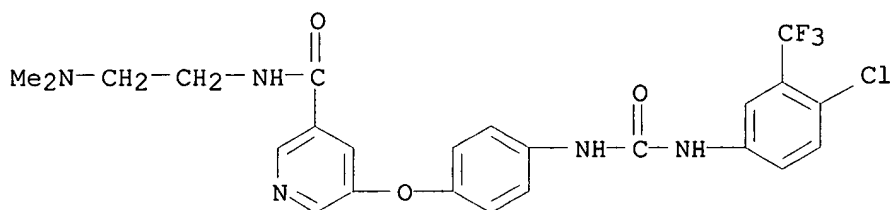
RN 284462-04-0 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



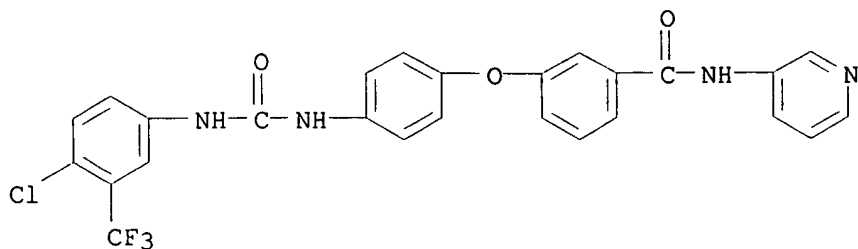
RN 284462-05-1 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



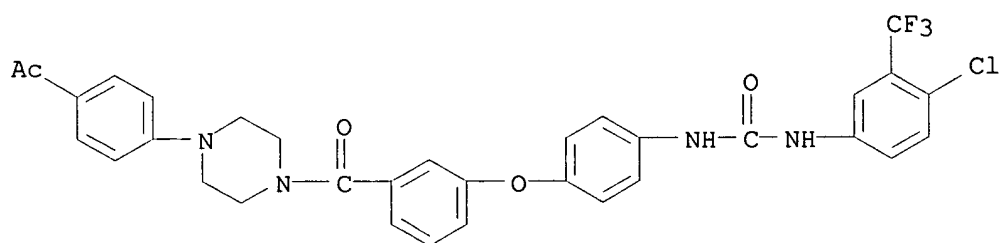
RN 284462-07-3 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]aminophenoxy]-N-3-pyridinyl- (9CI) (CA INDEX NAME)



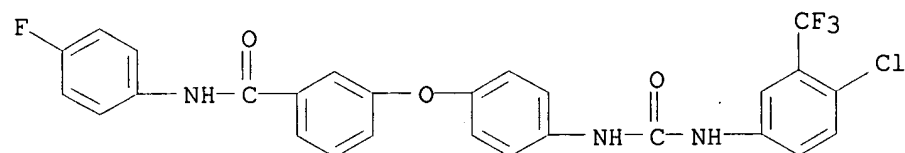
RN 284462-08-4 CAPLUS

CN Piperazine, 1-(4-acetylphenyl)-4-[3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]benzoyl]- (9CI) (CA INDEX NAME)



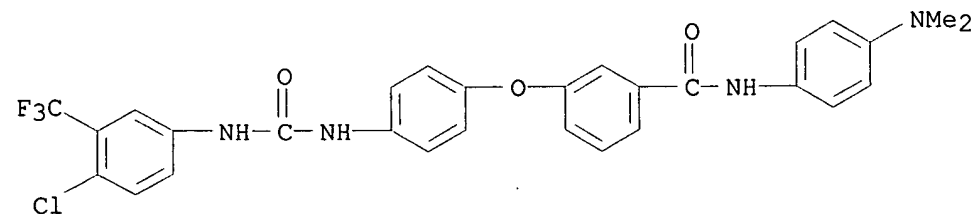
RN 284462-09-5 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



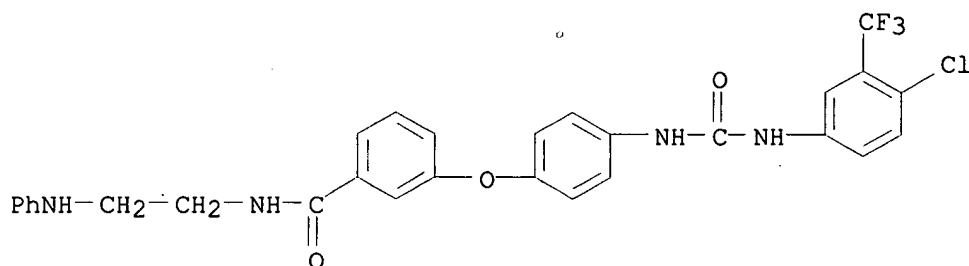
RN 284462-10-8 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-(dimethylamino)phenyl]- (9CI) (CA INDEX NAME)



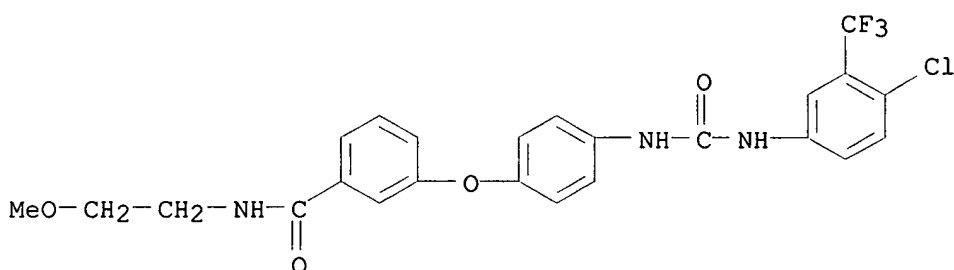
RN 284462-11-9 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(phenylamino)ethyl]- (9CI) (CA INDEX NAME)



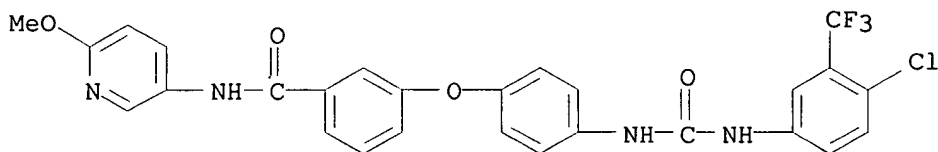
RN 284462-12-0 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]aminophenoxy]-N-(2-methoxyethyl)- (9CI) (CA INDEX NAME)



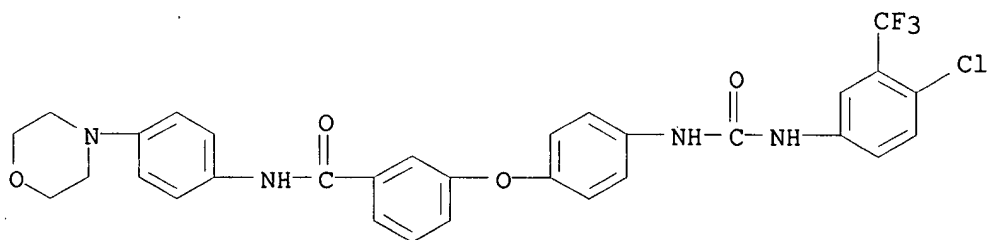
RN 284462-13-1 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]aminophenoxy]-N-(6-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



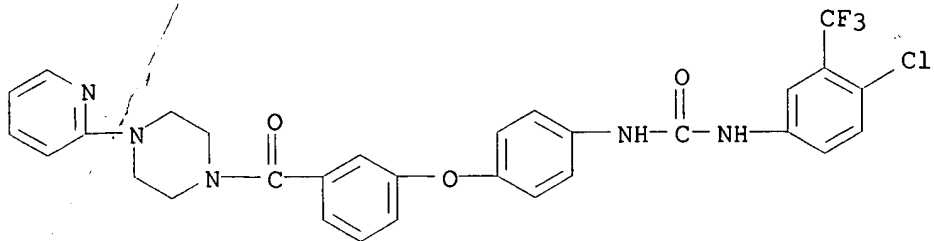
RN 284462-15-3 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]aminophenoxy]-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



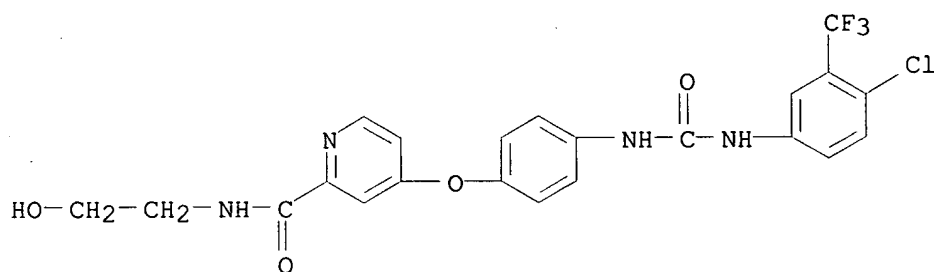
RN 284462-16-4 CAPLUS

CN Piperazine, 1-[3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]aminophenoxy]benzoyl]-4-(2-pyridinyl)- (9CI) (CA INDEX NAME)



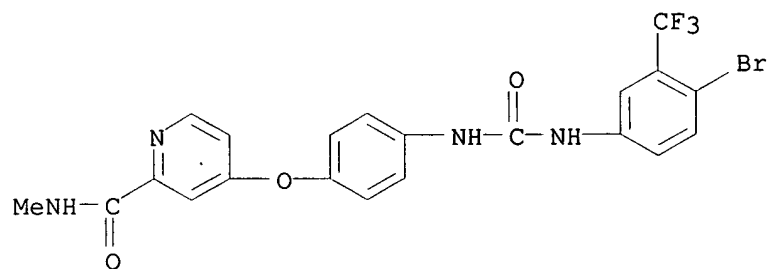
RN 284462-17-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



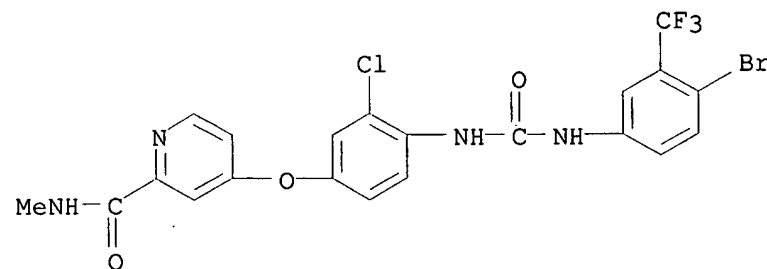
RN 284462-18-6 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



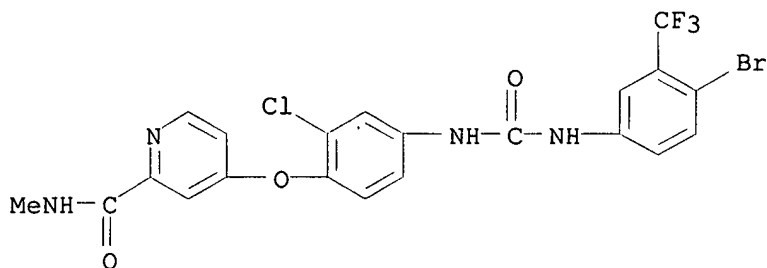
RN 284462-19-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-3-chlorophenoxy]-N-methyl- (9CI) (CA INDEX NAME)



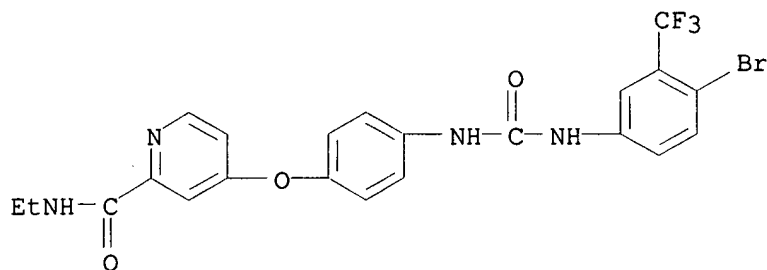
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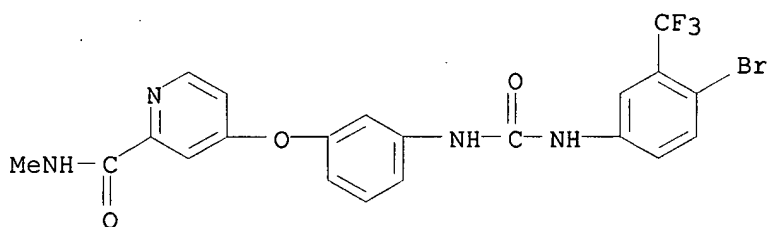
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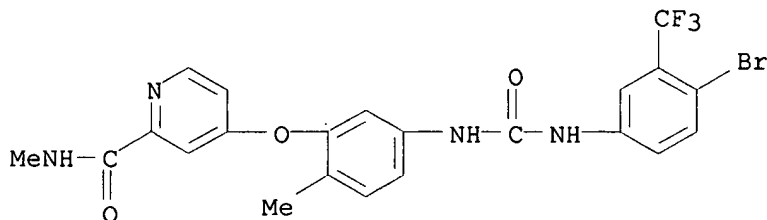
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CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

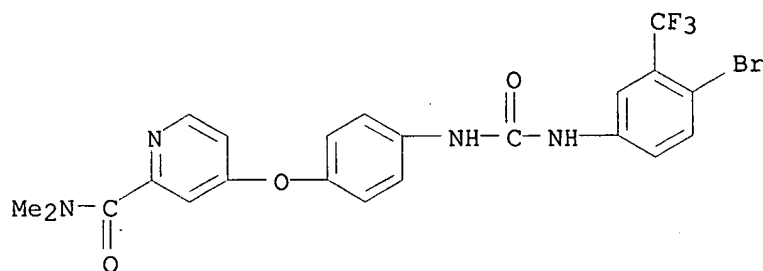


RN 284462-23-3 CAPLUS

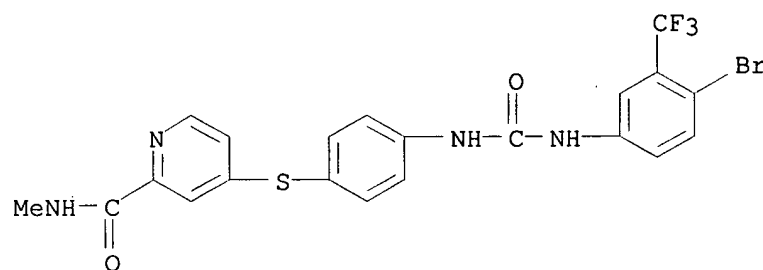
CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



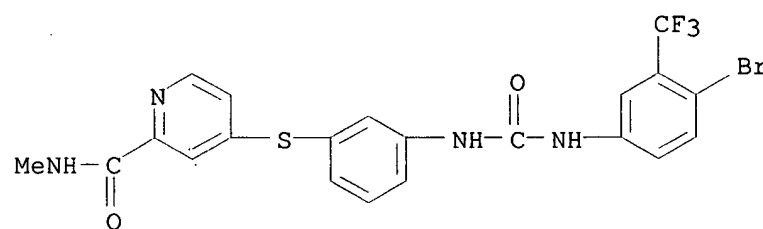
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CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



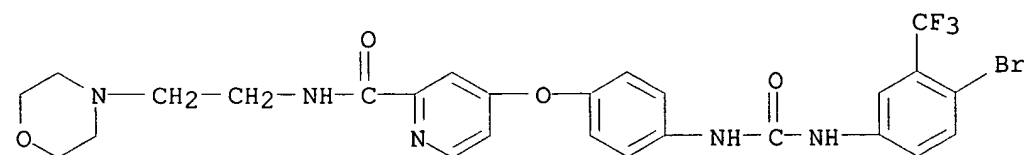
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CN 2-Pyridinecarboxamide, 4-[[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]c  
arbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



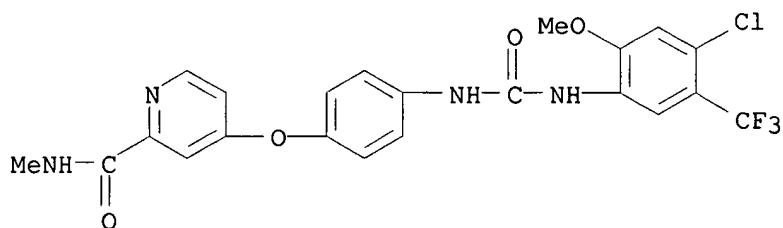
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CN	2-Pyridinecarboxamide, 4-[[[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]c arbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)	



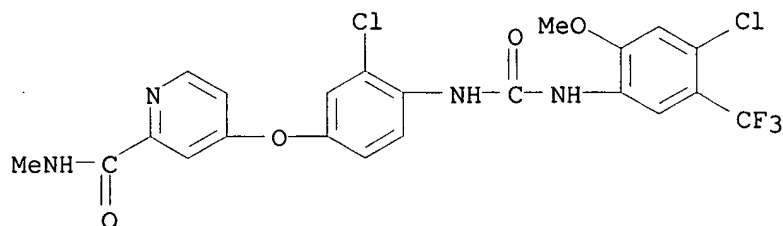
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CN	2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)	



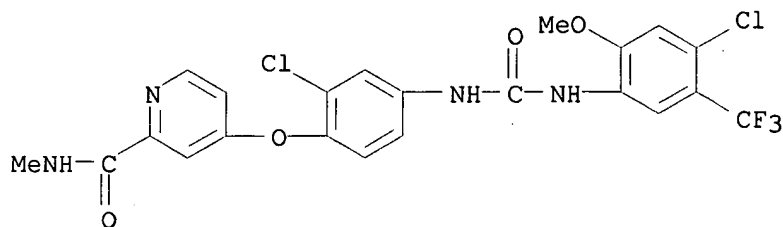
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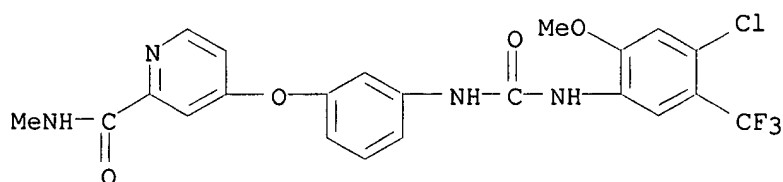
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CN 2-Pyridinecarboxamide, 4-[3-chloro-4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-30-2 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[2-chloro-4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

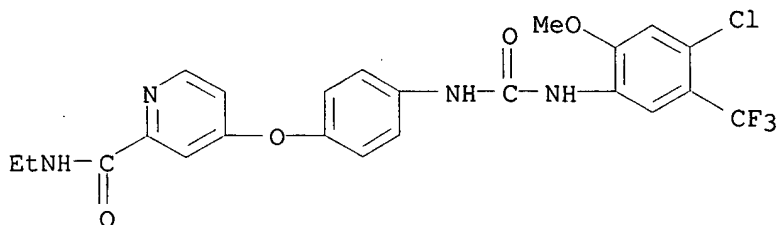


RN 284462-31-3 CAPLUS  
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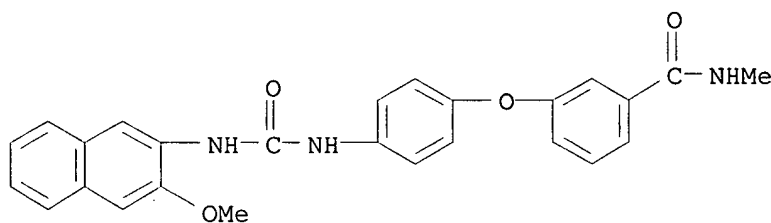
RN 284462-32-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-ethyl- (9CI) (CA INDEX NAME)



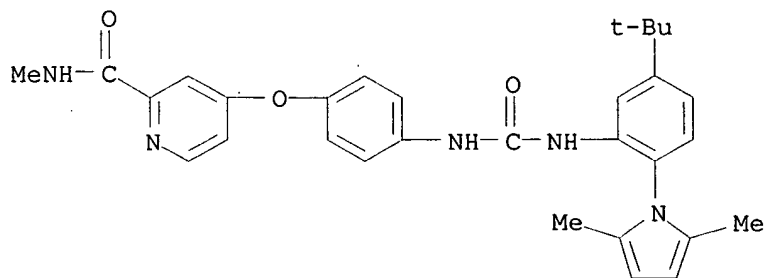
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CN Benzamide, 3-[4-[[[(3-methoxy-2-naphthalenyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



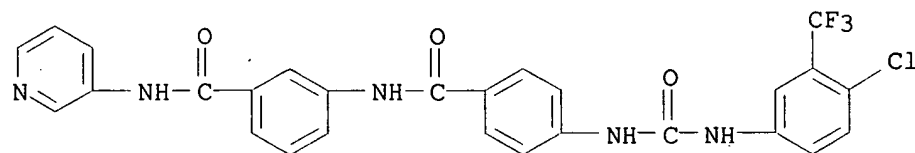
RN 284462-35-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[5-(1,1-dimethylethyl)-2-(2,5-dimethyl-1H-pyrrol-1-yl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-70-0 CAPLUS

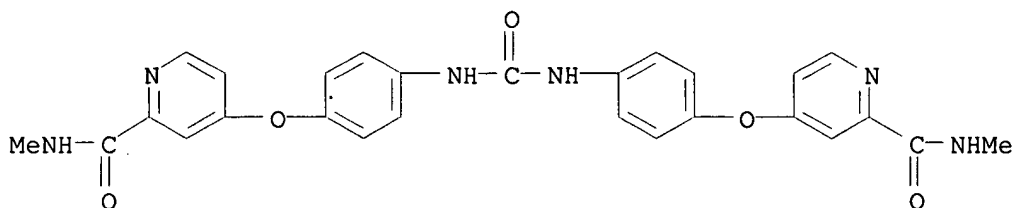
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RN 284670-98-0 CAPLUS

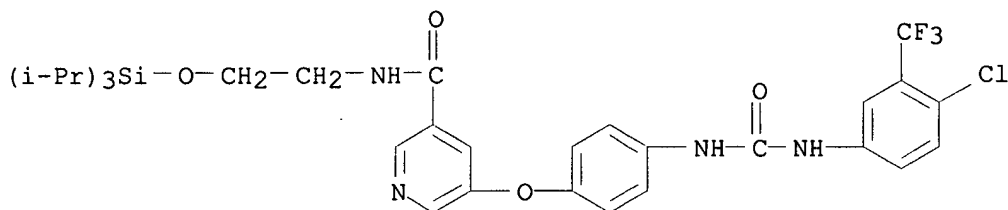


CN 2-Pyridinecarboxamide, 4,4'-[carbonylbis(imino-4,1-phenyleneoxy)]bis[N-methyl- (9CI) (CA INDEX NAME)



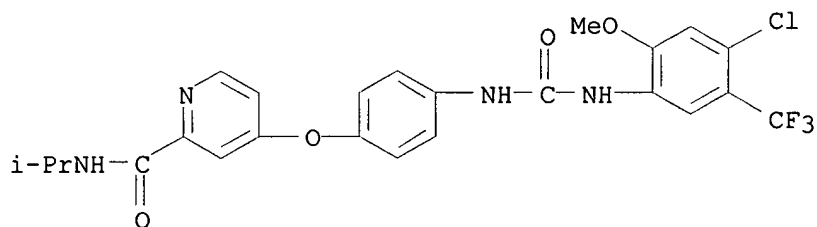
RN 447457-08-1 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-[[tris(1-methylethyl)silyl]oxy]ethyl]- (9CI) (CA INDEX NAME)



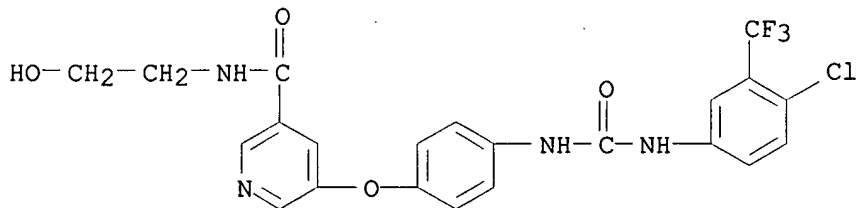
RN 447457-09-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



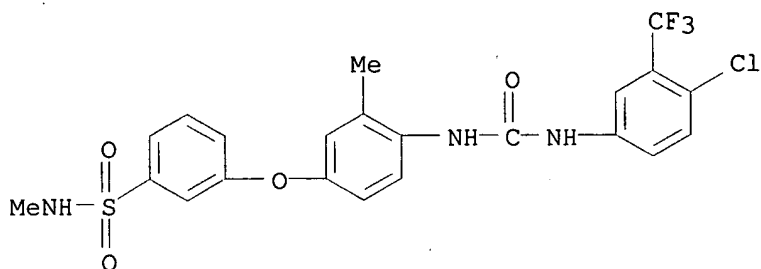
RN 474642-55-2 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



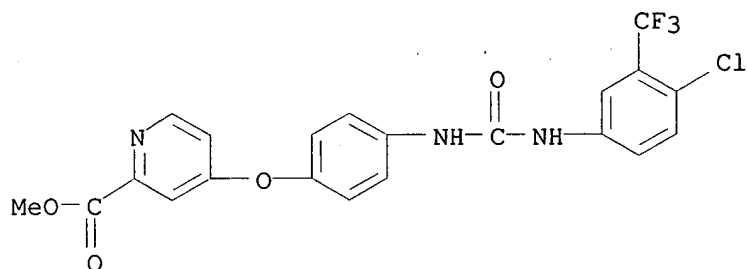
RN 573673-42-4 CAPLUS

CN Benzenesulfonamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-3-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



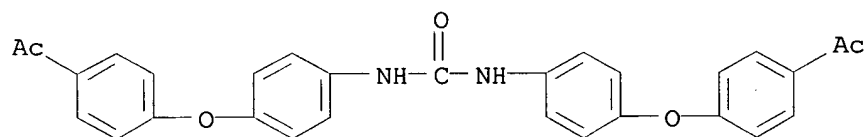
RN 573673-43-5 CAPLUS

CN 2-Pyridinecarboxylic acid, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
(CA INDEX NAME)



RN 573673-45-7 CAPLUS

CN Urea, N,N'-bis[4-(4-acetylphenoxy)phenyl]- (9CI) (CA INDEX NAME)



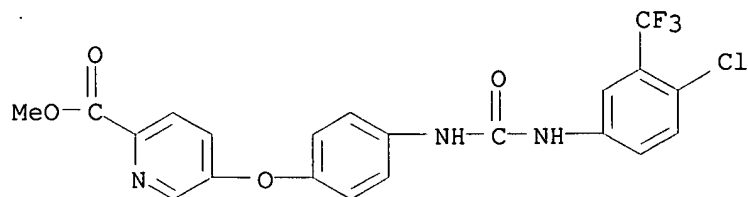
IT 284461-86-5 284462-06-2 284462-71-1

284462-76-6 573673-53-7 573673-59-3

RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of diphenylureas as RAF kinase inhibitors)

RN 284461-86-5 CAPLUS

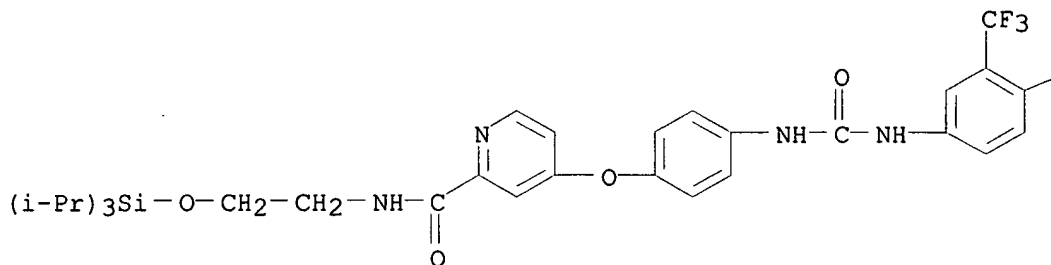
CN 2-Pyridinecarboxylic acid, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
(CA INDEX NAME)



RN 284462-06-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-[[tris(1-methylethyl)silyl]oxy]ethyl]- (9CI)  
(CA INDEX NAME)

PAGE 1-A

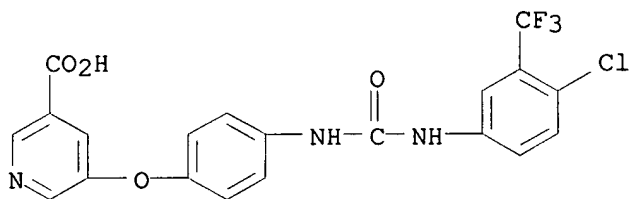


PAGE 1-B

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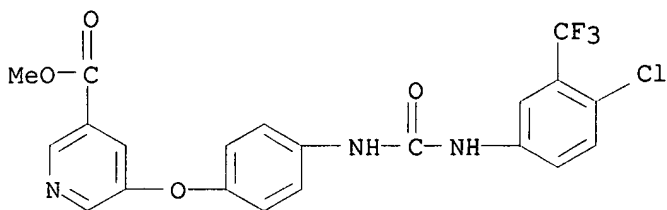
RN 284462-71-1 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



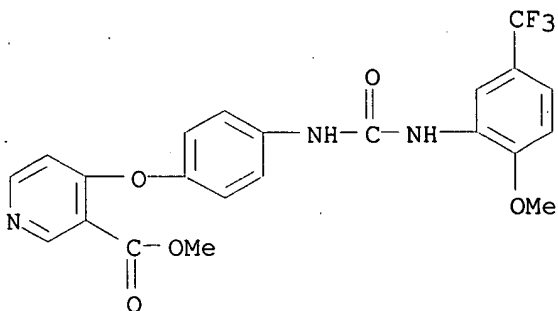
RN 284462-76-6 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
(CA INDEX NAME)



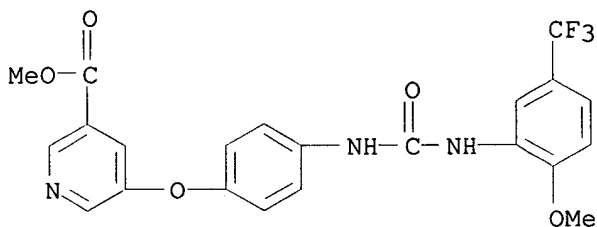
RN 573673-53-7 CAPLUS

CN 3-Pyridinecarboxylic acid, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
(CA INDEX NAME)



RN 573673-59-3 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
(CA INDEX NAME)

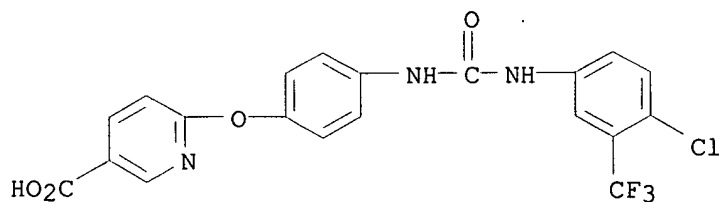


IT 573673-47-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of diphenylureas as RAF kinase inhibitors)

RN 573673-47-9 CAPLUS

CN 3-Pyridinecarboxylic acid, 6-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



L122 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:736198 CAPLUS

DOCUMENT NUMBER: 139:301125

TITLE: BAY-43-9006 (Bayer/Onyx)

AUTHOR(S): Lee, John T.; McCubrey, James A.

CORPORATE SOURCE: Department of Microbiology and Immunology, Brody School of Medicine at East Carolina University, Greenville, NC, 27858-4353, USA

SOURCE: Current Opinion in Investigational Drugs (Thomson Current Drugs) 2003, 4(6), 757-763

CODEN: COIDAZ; ISSN: 1472-4472

PUBLISHER: Thomson Current Drugs

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

ED Entered STN: 19 Sep 2003

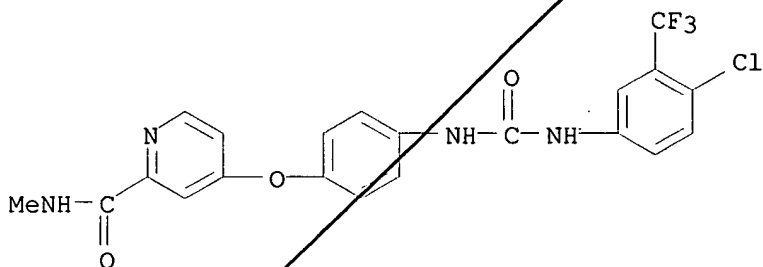
AB A review. Bayer and Onyx are developing BAY-43-9006, an oral cytostatic Raf kinase inhibitor for the potential treatment of colorectal and breast cancers, hepatocellular carcinoma and non-small-cell lung cancer, in addn. to acute myelogenous leukemia, myelodysplastic syndrome and other cancers. A US IND was filed in May 2000 and by Feb. 2003 BAY-43-9006 was in phase II trials, with phase III trials expected to begin later in 2003.

IT 284461-73-0, BAY 43-9006

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BAY 43-9006 for treatment of cancer patients)

RN 284461-73-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



IT 139691-76-2, Raf kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitor; BAY 43-9006 for treatment of cancer patients)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L122 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:12708 CAPLUS

DOCUMENT NUMBER: 140:70551

TITLE: A Phase I clinical and pharmacokinetic study of the Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors

AUTHOR(S): Richly, H.; Kupsch, P.; Passage, K.; Grubert, M.; Hilger, R. A.; Kredtke, S.; Voliotis, D.; Scheulen, M. E.; Seeber, S.; Strumberg, D.

CORPORATE SOURCE: West German Cancer Center, University of Essen, Essen, Germany

SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2003), 41(12), 620-621  
CODEN: IJCTHEK; ISSN: 0946-1965

PUBLISHER: Dustri-Verlag Dr. Karl Feistle

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 08 Jan 2004

AB Objective: The primary objective of this phase I study was to define the safety profile of BAY 43-9006 administered in combination with doxorubicin. Patients and methods: Twenty-nine patients with advanced,

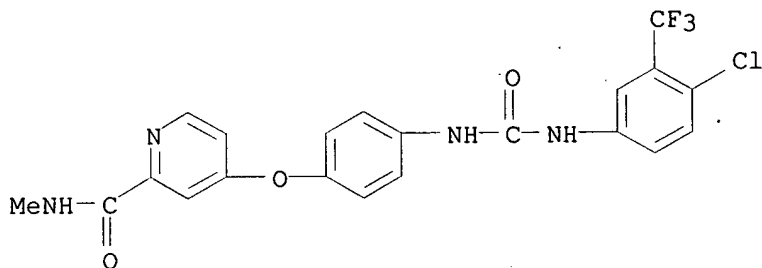
refractory solid tumors were treated with doxorubicin (60mg/m2) every 3 wk for 6 consecutive cycles. BAY 43-9006 in combination with doxorubicin chemotherapy was administered at 3 dose levels. Results: Toxicity and response were evaluable in a total of 24 out of 29 enrolled patients. Dose-limiting toxicity was obsd. at various dose levels. Doxorubicin plasma Cmax/AUC values increased on escalating the dose of BAY 43-9006. Patients with liver metastases and elevated values of AST and conjugated bilirubin, compared to patients with normal hepatic function, showed a higher AUC for doxorubicin at all dose levels. Conclusions: Our data suggest a pharmacol. interaction of BAY 43-9006 at DL 400 mg bid with doxorubicin resulting in significantly increased AUC for doxorubicin.

IT 284461-73-0, BAY 43-9006

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (clin. and pharmacokinetic study of Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors)

RN 284461-73-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



IT 139691-76-2, Raf kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor; clin. and pharmacokinetic study of Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L122 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:12707 CAPLUS

DOCUMENT NUMBER: 146-70550

TITLE: Drug-drug interaction pharmacokinetic study with the Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (OPT-11) in patients with solid tumors

AUTHOR(S): Mross, K.; Steinbild, S.; Baas, F.; Reil, M.; Buss, P.; Mersmann, S.; Voliotis, D.; Schwartz, B.; Brendel, E.

CORPORATE SOURCE: Tumor Biology Center at the Albert-Ludwigs-University Freiburg, Leverkusen, Germany

SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2003), 41(12), 618-619

CODEN: ICTHEK; ISSN: 0946-1965

PUBLISHER: Dustri-Verlag Dr. Karl Feistle

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 08 Jan 2004

AB Classical cytotoxic anticancer drugs generally have specific actions but also interfere with signalling pathways. A logical approach is therefore to combine the Raf kinase inhibitor (RKI) with classical cytotoxic agents since recent work has shown that the RKI BAY 43-9006 and CPT-11 have additive or synergistic actions. Objective: Because a pharmacol. drug-drug interaction cannot be ruled out, interaction studies were started using the RKI BAY 43-9006 in combination with the most important anticancer drugs, such as CPT-11. Patients and methods: The study protocol included three groups of 6 patients with solid tumors given different RKI doses and the same dosage of CPT-11. Blood samples for measurement of CPT-11 and SN-38 were obtained both during and in the absence of RKI treatment. Results: Ests. of toxicity, response and pharmacokinetics during the first RKI dose could be made in a total of 9/18 patients. All symptoms of toxicity were considered to be due to CPT-11 or RKI. The PK evaluation showed no significant differences for CPT-11 and SN-38, with or without RKI. Conclusions: The combination CPT-11 and SN-38 PK is not significantly influenced by the addn. of RKI. There is no indication that the PK of RKI are influenced significantly by CPT-11 and SN-38.

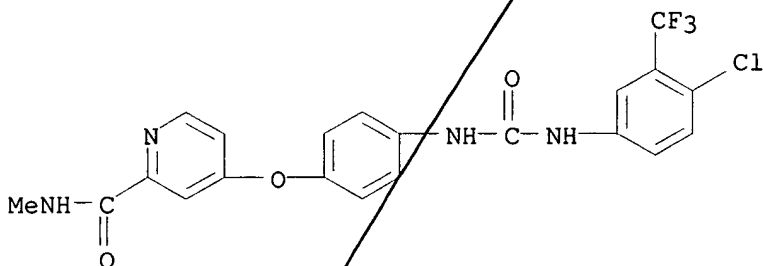
IT 284461-73-0, BAY 43-9006

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug-drug interaction pharmacokinetic study with Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors)

RN 284461-73-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



IT 139691-76-2, Raf kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor; drug-drug interaction pharmacokinetic study with Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L122 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:476541 CAPLUS

DOCUMENT NUMBER: 139:143192

TITLE: Activity of the Raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors

AUTHOR(S): DeGrendele, Heather

CORPORATE SOURCE: USA  
SOURCE: Clinical Colorectal Cancer (2003), 3(1), 16-18  
CODEN: CCCLCF; ISSN: 1533-0028  
PUBLISHER: Cancer Information Group  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

ED Entered STN: 23 Jun 2003

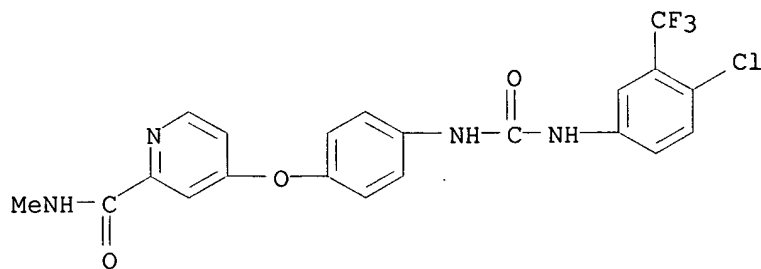
AB A review. BAY 43-9006 is the first orally active Raf kinase inhibitor to undergo clin. testing and has shown promise in the treatment of colorectal cancer. Treatment with BAY 43-9006 has resulted in stable disease in 37 % of patients across this phase I series, with 42 % of colorectal cancer patients achieving stable disease. Among patients achieving stable disease, 27 have been on therapy for over 6 mo without progression. Toxicity assocd. with this regimen is mild, with few grade 3/4 adverse events reported. Furthermore, fluorescence-activated cell sorter (FACS) anal. demonstrated that treatment with BAY 43-9006 could result in the inhibition of extracellular signal-regulated kinase (ERK) activation. Based on this phase I data, 2 phase II trials, including one in patients with colorectal cancer, have been initiated, and phase III trials are planned for 2003. At the 38th Annual Meeting of the American Society of Clin. Oncol., Vincent and colleagues reported on preclin. studies combining BAY 43-9006 with irinotecan, vinorelbine, or gemcitabine in human xenografts models. They demonstrated that BAY 43-9006 combined with cytotoxic or cytostatic agents is at least as efficacious as the individual agents administered alone. With this as rationale, multiple phase I/II studies are being designed to investigate the role of BAY 43-9006 in combination with std. chemotherapy.

IT 284461-73-0, BAY 43-9006

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(activity of Raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors)

RN 284461-73-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



IT 139691-76-2, Raf kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitor; activity of Raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

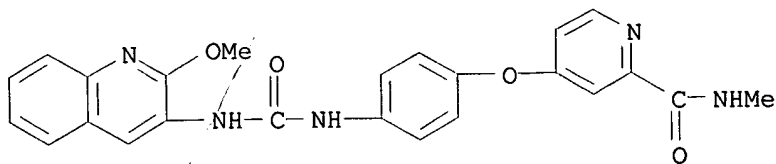
L122 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:832761 CAPLUS



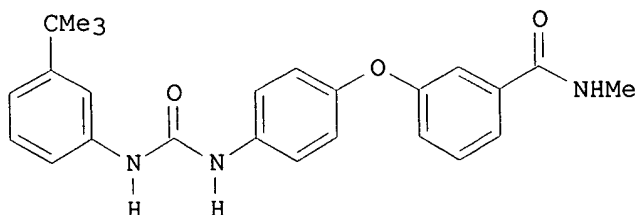
DOCUMENT NUMBER: 137:337791  
TITLE: Preparation of quinolyl, isoquinolyl or pyridyl-ureas  
as inhibitors of raf kinase  
INVENTOR(S): Dumas, Jacques; Riedl, Bernd; Khire, Uday; Sibley,  
Robert N.; Hatoum-Mokdad, Holia; Monahan,  
Mary-Katherine; Gunn, David E.; Lowinger, Timothy B.;  
Scott, William J.; Smith, Roger A.; Wood, Jill E.  
PATENT ASSIGNEE(S): Bayer Corporation, USA  
SOURCE: PCT Int. Appl., 65 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085857	A2	20021031	WO 2002-US12066	20020418
WO 2002085857	A3	20030116		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1379505	A2	20040114	EP 2002-725710	20020418
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:		US 2001-838285	A	20010420
		WO 2002-US12066	W	20020418
OTHER SOURCE(S): MARPAT 137:337791				
ED	Entered STN: 01 Nov 2002			
AB	Title compds. A-D-B (I) [D = NHCONH; A = (un)substituted t-butylpyridyl, etc.; B = (un)substituted bridged cyclic structure, etc.] and analogs were prepd. For instance, 4-tert-butyl-2-aminopyridine was coupled to 4-(4-pyridylmethyl)aniline (CH <sub>2</sub> Cl <sub>2</sub> , CDI, 0.degree.) to give N-(4-tert-butylpyridyl)-N'-[4-(4-pyridinylmethyl)phenyl]urea as a white solid. Example compds. had IC <sub>50</sub> between 10nM and 10.mu.M for raf kinase. I are useful for the treatment of cancerous cell growth mediated by raf kinase.			
IT	139691-76-2, Raf kinase			
	RL: BSU (Biological study, unclassified); BIOL (Biological study) (prepn. of quinolyl, isoquinolyl or pyridyl-ureas as <b>inhibitors</b> of raf kinase)			
RN	139691-76-2 CAPLUS			
CN	Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)			
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***				
IT	432050-22-1P			
	RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf kinase)			
RN	432050-22-1 CAPLUS			
CN	2-Pyridinecarboxamide, 4-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amin o]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)			



L122 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2002:615574 CAPLUS  
 DOCUMENT NUMBER: 137:169425  
 TITLE: Preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors  
 INVENTOR(S): Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Sibley, Robert N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.  
 PATENT ASSIGNEE(S): Bayer Corporation, USA  
 SOURCE: PCT Int. Appl., 125 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062763	A2	20020815	WO 2002-US3361	20020207
WO 2002062763	A3	20021010		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002165394	A1	20021107	US 2001-777920	20010207
PRIORITY APPLN. INFO.:				
			US 2001-777920	A 20010207
			US 1999-115877P	P 19990113
			US 1999-257266	B2 19990225
			US 1999-425228	B2 19991022
			US 2001-758548	A2 20010112
OTHER SOURCE(S): MARPAT 137:169425				
ED Entered STN: 16 Aug 2002				
GI				



II

AB Title compds., e.g., RNHCONHZOR1 [I; R = C6H4(CMe3)-3,

2-methoxy-5-trifluoromethylphenyl, 4-chloro-3-trifluoromethylphenyl, 2-methoxy-3-quinolyl, etc.; R1 = (un)substituted acylphenyl, -acylpyridinyl, etc.; Z = (un)substituted 1,3- or -1,4-phenylene] were prepd. Thus, 4-(H2N)C6H4OC6H4(CONHMe)-4 (prepn. given) was condensed with 3-(Me3C)C6H4NH2 and CO(OCCl3)2 to give title compd. II. Data for biol. activity of title compds. were given.

IT 139691-76-2, Raf kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (mediated disorders; treatment; prepn. of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

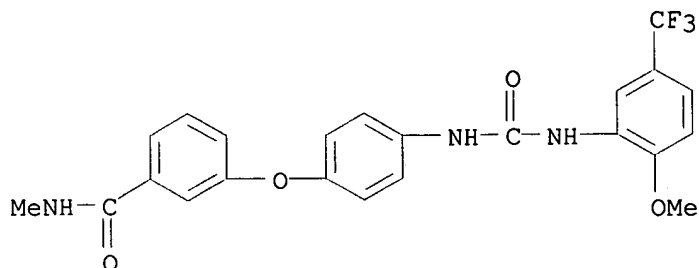
IT 228418-48-2P 284461-33-2P 284461-34-3P  
284461-35-4P 284461-36-5P 284461-37-6P  
284461-40-1P 284461-41-2P 284461-42-3P  
284461-43-4P 284461-44-5P 284461-45-6P  
284461-46-7P 284461-47-8P 284461-48-9P  
284461-49-0P 284461-50-3P 284461-51-4P  
284461-52-5P 284461-53-6P 284461-55-8P  
284461-57-0P 284461-58-1P 284461-60-5P  
284461-61-6P 284461-62-7P 284461-63-8P  
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284461-67-2P 284461-68-3P 284461-69-4P  
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284461-76-3P 284461-78-5P 284461-79-6P  
284461-80-9P 284461-81-0P 284461-82-1P  
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)

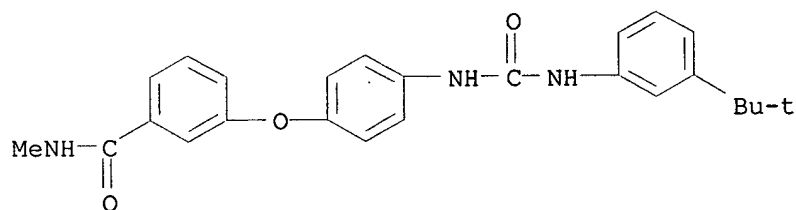
RN 228418-48-2 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



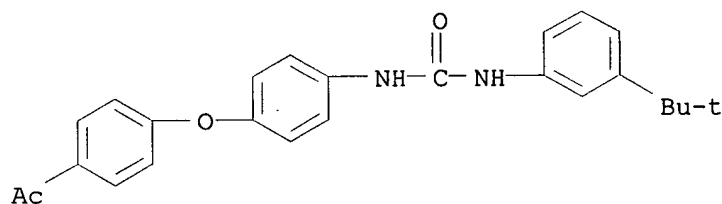
RN 284461-33-2 CAPLUS

CN Benzamide, 3-[4-[[[3-(1,1-dimethylethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



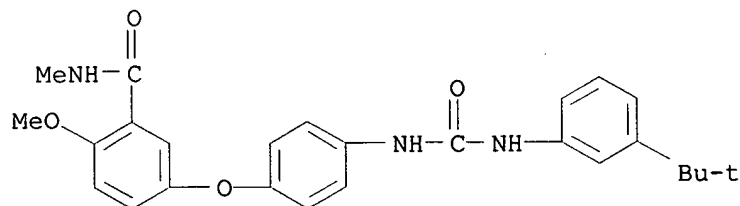
RN 284461-34-3 CAPLUS

CN Urea, N-[4-(4-acetylphenoxy)phenyl]-N'-[3-(1,1-dimethylethyl)phenyl]- (9CI) (CA INDEX NAME)



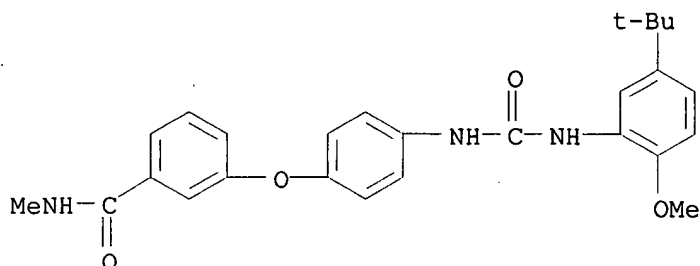
RN 284461-35-4 CAPLUS

CN Benzamide, 5-[4-[[[3-(1,1-dimethylethyl)phenyl]amino]carbonyl]amino]phenoxy]-2-methoxy-N-methyl- (9CI) (CA INDEX NAME)



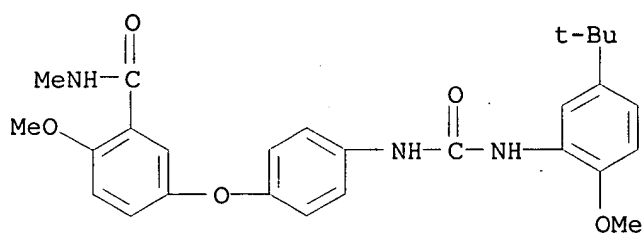
RN 284461-36-5 CAPLUS

CN Benzamide, 3-[4-[[[5-(1,1-dimethylethyl)-2-methoxyphenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



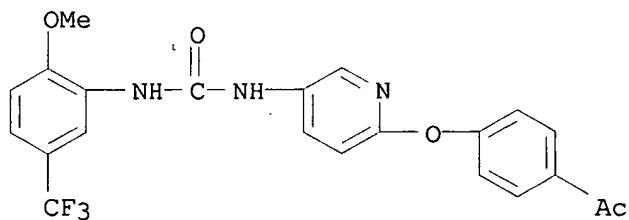
RN 284461-37-6 CAPLUS

CN Benzamide, 5-[4-[[[5-(1,1-dimethylethyl)-2-methoxyphenyl]amino]carbonyl]amino]phenoxy]-2-methoxy-N-methyl- (9CI) (CA INDEX NAME)



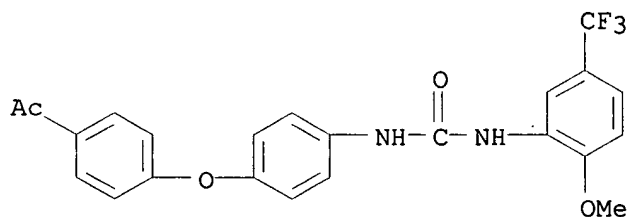
RN 284461-40-1 CAPLUS

CN Urea, N-[6-(4-acetylphenoxy)-3-pyridinyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



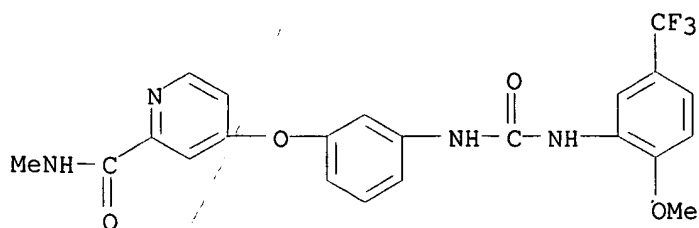
RN 284461-41-2 CAPLUS

CN Urea, N-[4-(4-acetylphenoxy)phenyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



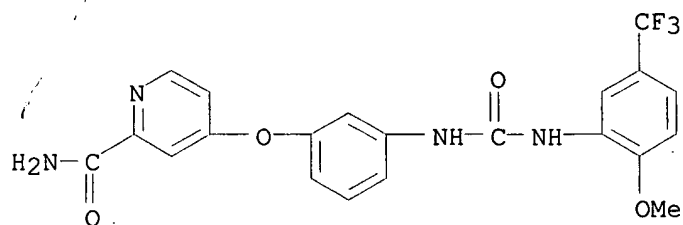
RN 284461-42-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



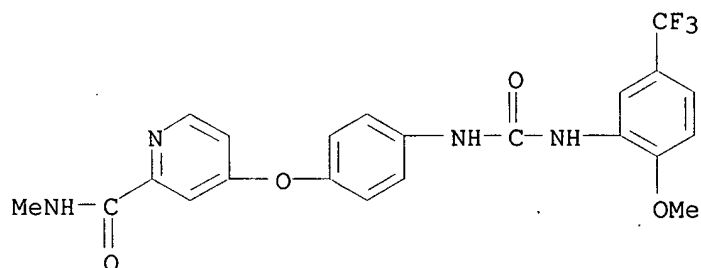
RN 284461-43-4 CAPLUS

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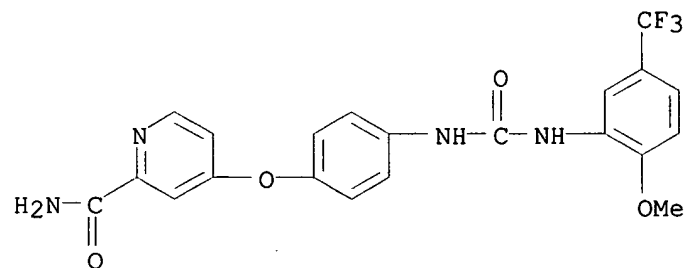
RN 284461-44-5 CAPLUS

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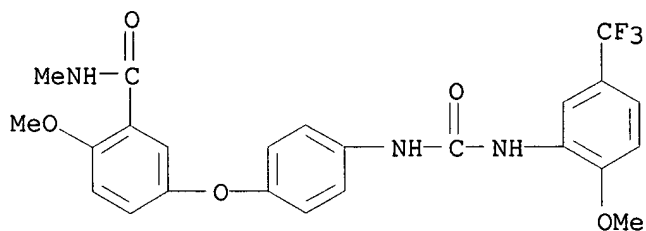
RN 284461-45-6 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



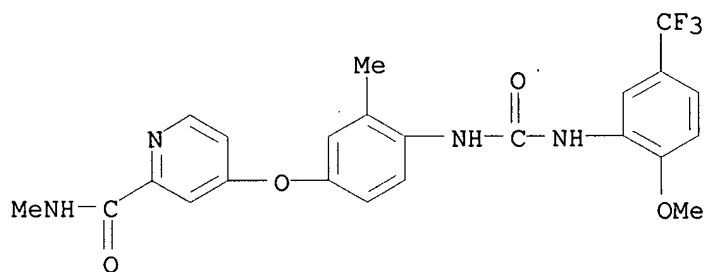
RN 284461-46-7 CAPLUS

CN Benzamide, 2-methoxy-5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



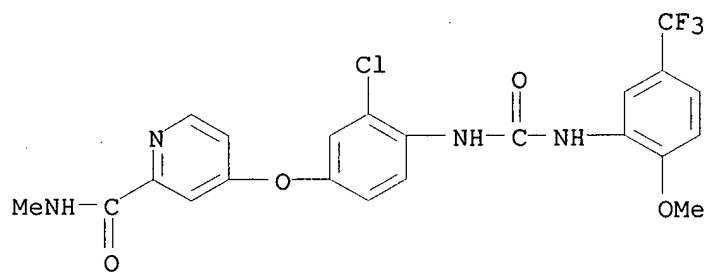
RN 284461-47-8 CAPLUS

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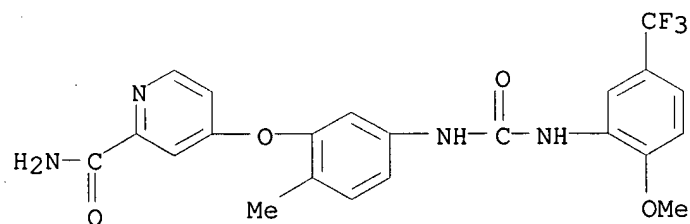
RN 284461-48-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-chloro-4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-49-0 CAPLUS

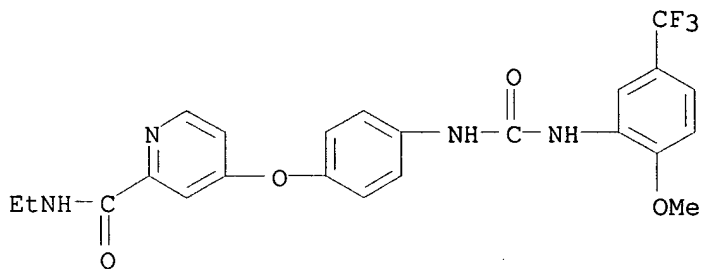
CN 2-Pyridinecarboxamide, 4-[5-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-50-3 CAPLUS

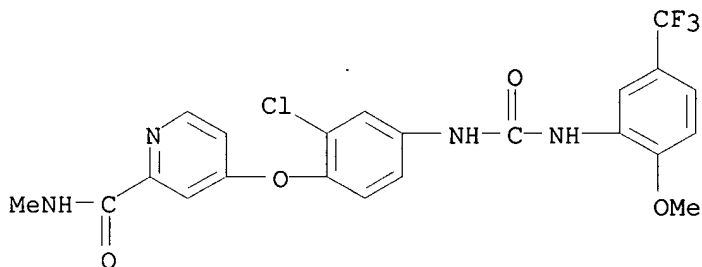
CN 2-Pyridinecarboxamide, N-ethyl-4-[4-[[[2-methoxy-5-

(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



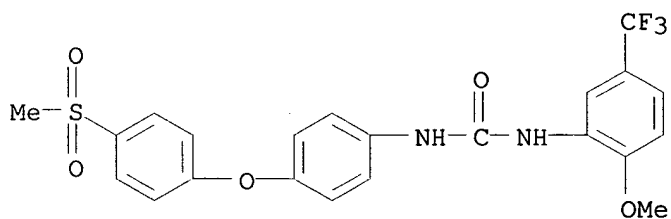
RN 284461-51-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[2-chloro-4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-52-5 CAPLUS

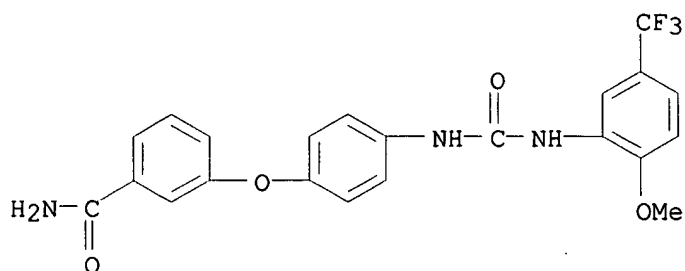
CN Urea, N-[2-methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[4-(methylsulfonyl)phenoxy]phenyl]- (9CI) (CA INDEX NAME)



RN 284461-53-6 CAPLUS

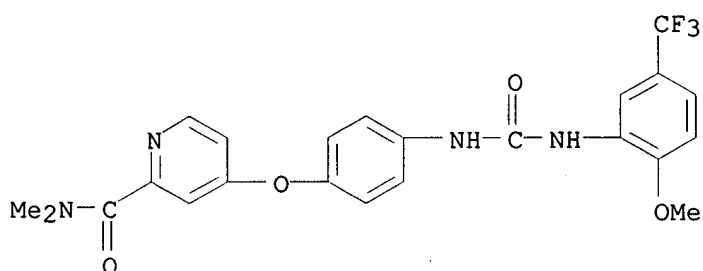
CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)





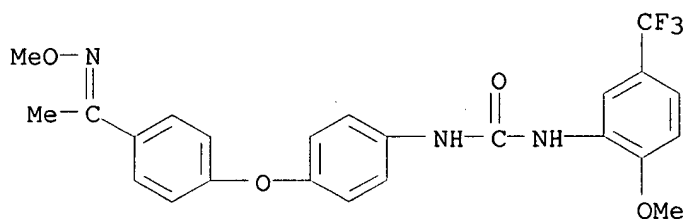
RN 284461-55-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



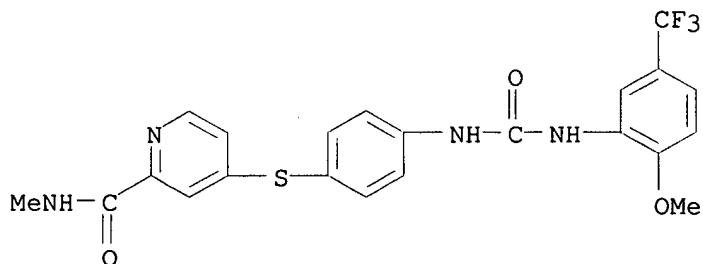
RN 284461-57-0 CAPLUS

CN Urea, N-[4-[4-[1-(methoxyimino)ethyl]phenoxy]phenyl]-N'-[2-methoxy-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



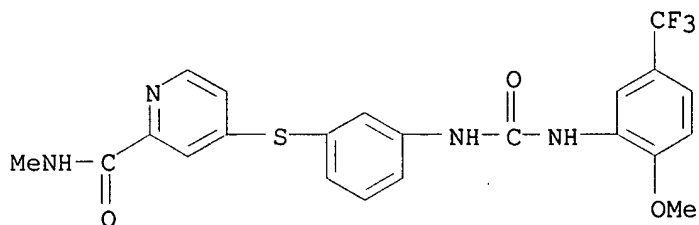
RN 284461-58-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



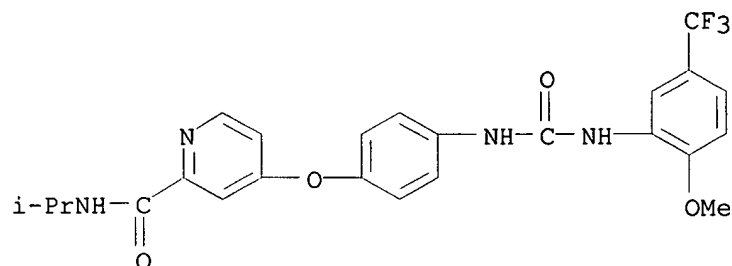
RN 284461-60-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



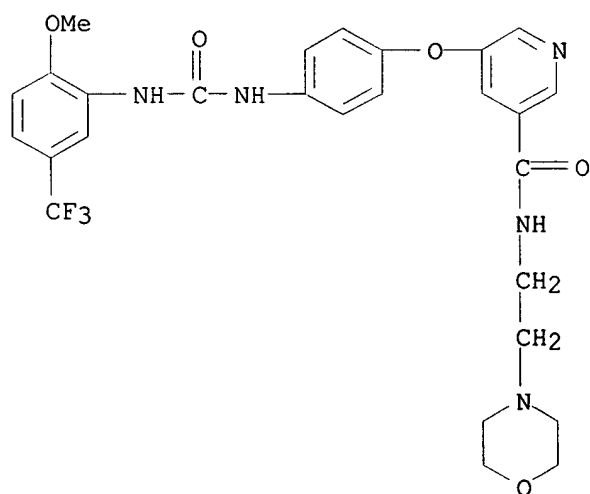
RN 284461-61-6 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



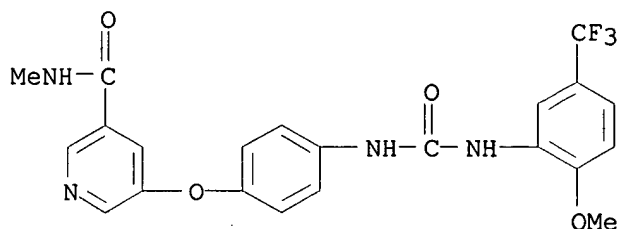
RN 284461-62-7 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



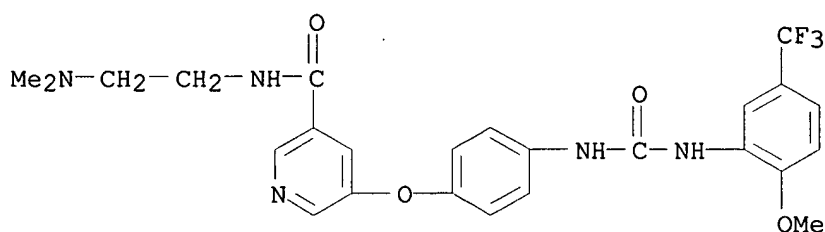
RN 284461-63-8 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



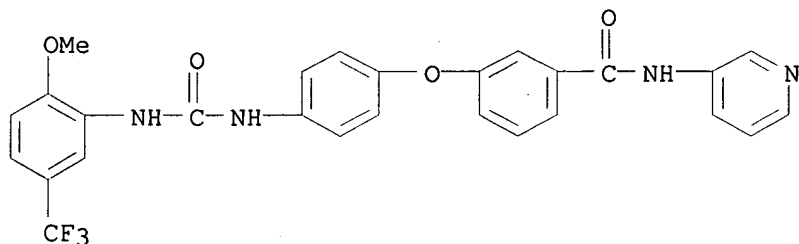
RN 284461-64-9 CAPLUS

CN 3-Pyridinecarboxamide, N-[2-(dimethylamino)ethyl]-5-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



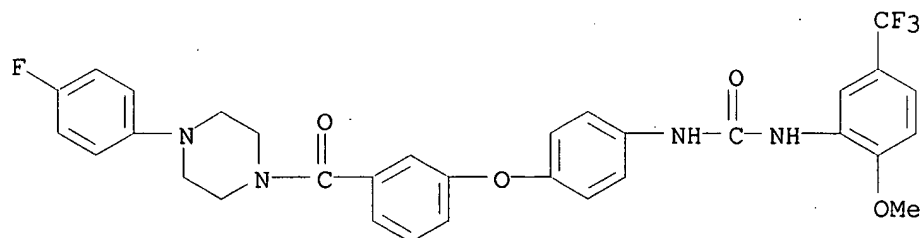
RN 284461-65-0 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-3-pyridinyl- (9CI) (CA INDEX NAME)



RN 284461-66-1 CAPLUS

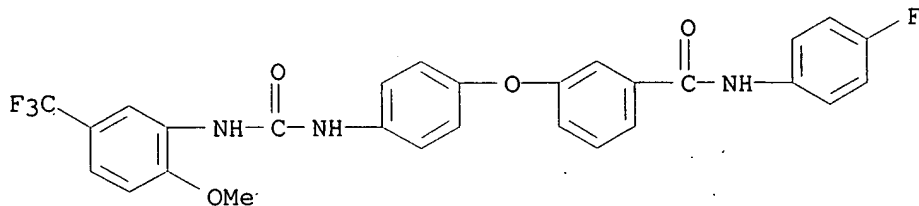
CN Piperazine, 1-(4-fluorophenyl)-4-[3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]benzoyl]- (9CI) (CA INDEX NAME)



RN 284461-67-2 CAPLUS

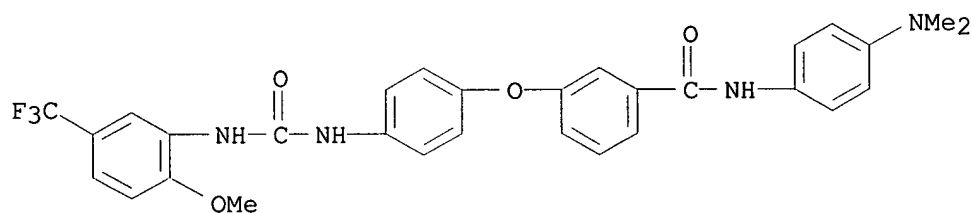
CN Benzamide, N-(4-fluorophenyl)-3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)

NAME)



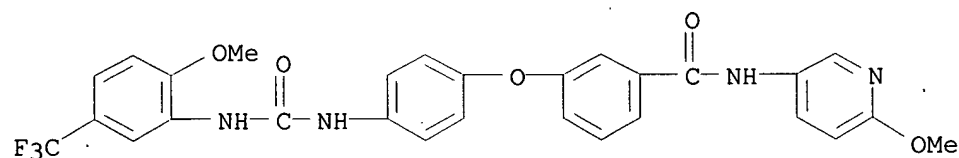
RN 284461-68-3 CAPLUS

CN Benzamide, N-[4-(dimethylamino)phenyl]-3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



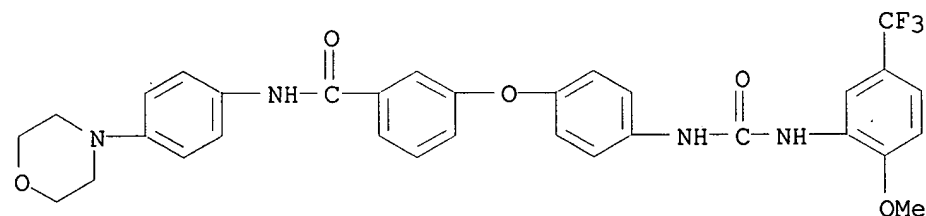
RN 284461-69-4 CAPLUS

CN Benzamide, N-(6-methoxy-3-pyridinyl)-3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



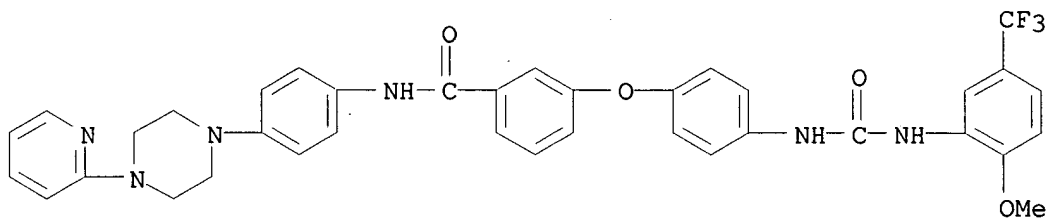
RN 284461-70-7 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



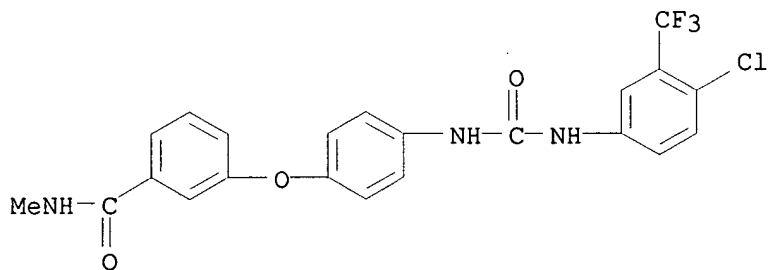
RN 284461-71-8 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-[4-(2-pyridinyl)-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



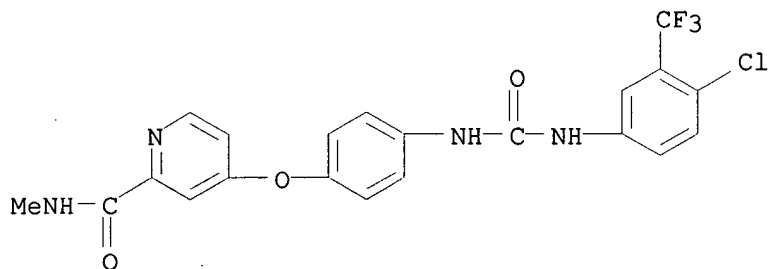
RN 284461-72-9 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



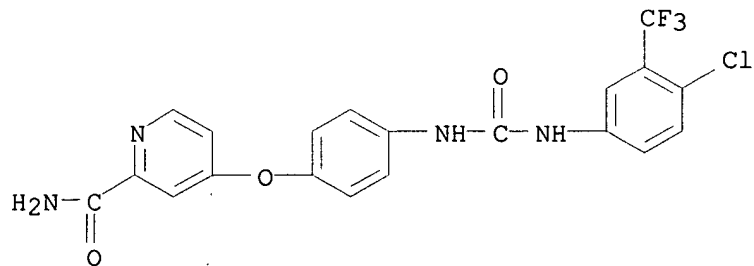
RN 284461-73-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



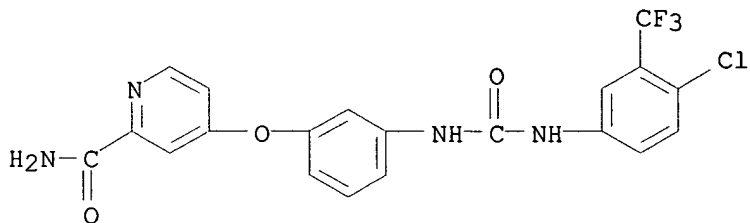
RN 284461-74-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



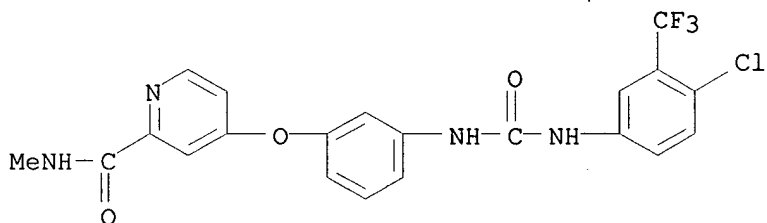
RN 284461-75-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



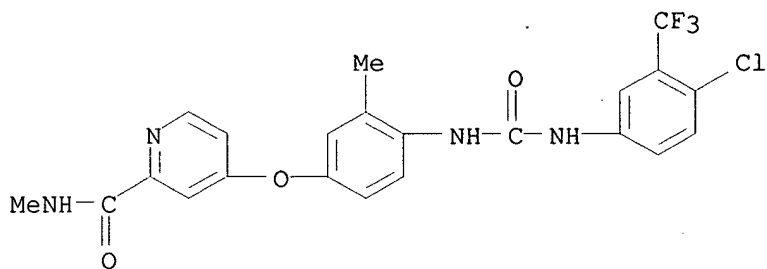
RN 284461-76-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



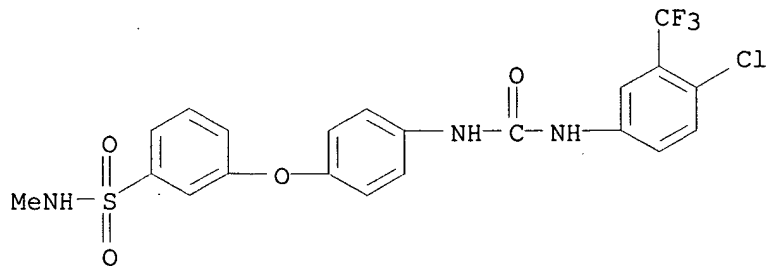
RN 284461-78-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-3-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)

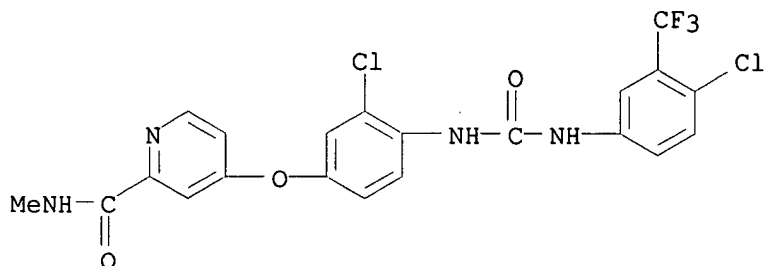


RN 284461-79-6 CAPLUS

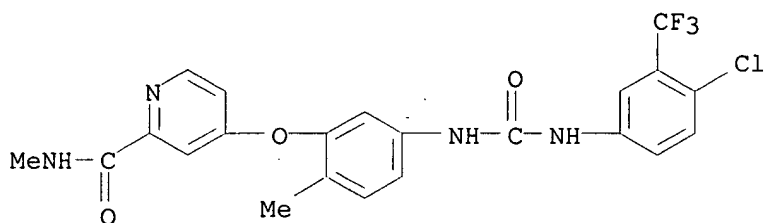
CN Benzenesulfonamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



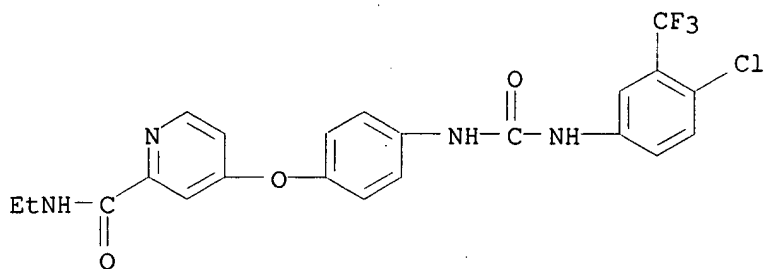
RN 284461-80-9 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[3-chloro-4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



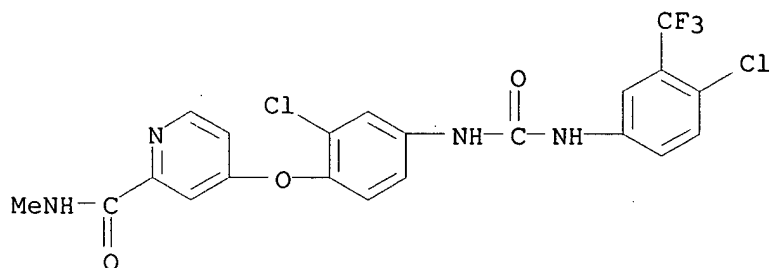
RN 284461-81-0 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-82-1 CAPLUS  
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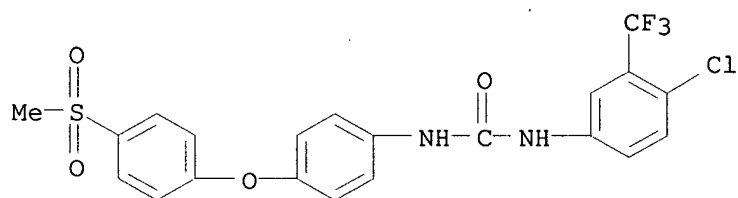


RN 284461-83-2 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[2-chloro-4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



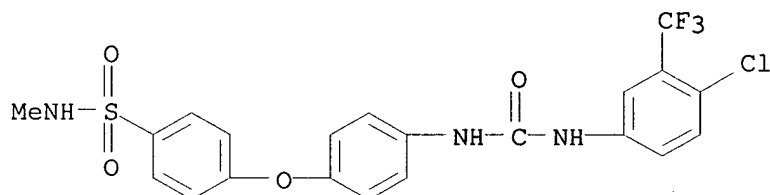
RN 284461-84-3 CAPLUS

CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[4-(methylsulfonyl)phenoxy]phenyl]- (9CI) (CA INDEX NAME)



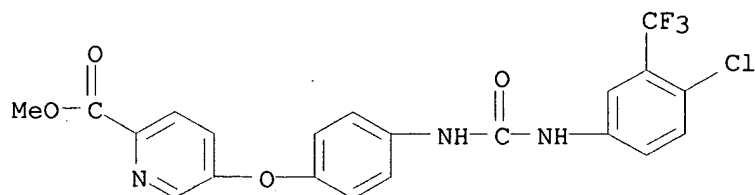
RN 284461-85-4 CAPLUS

CN Benzenesulfonamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-86-5 CAPLUS

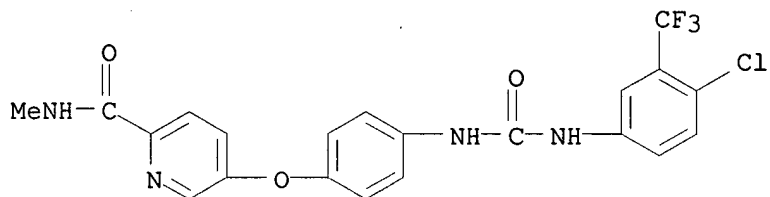
CN 2-Pyridinecarboxylic acid, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 284461-88-7 CAPLUS

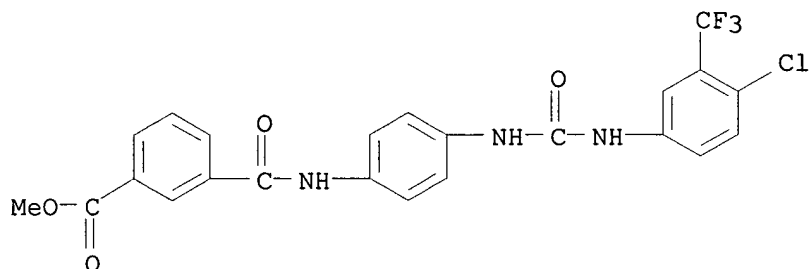
CN 2-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)





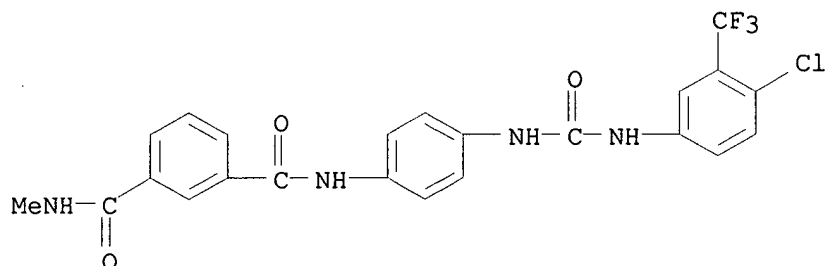
RN 284461-89-8 CAPLUS

CN Benzoic acid, 3-[[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]amino]carbonyl-, methyl ester (9CI) (CA INDEX NAME)



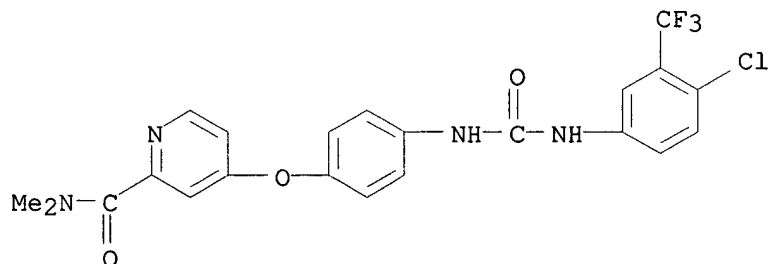
RN 284461-90-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]-N'-methyl- (9CI) (CA INDEX NAME)



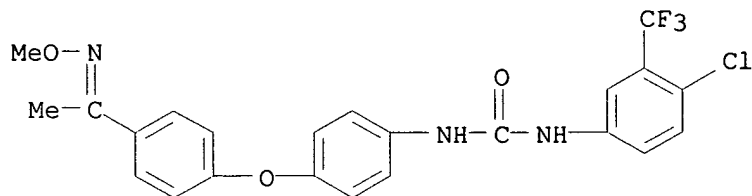
RN 284461-91-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



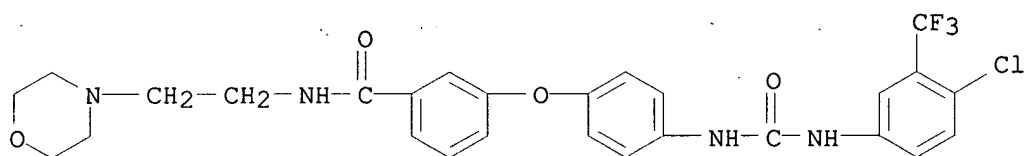
RN 284461-92-3 CAPLUS

CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[4-[1-(methoxyimino)ethyl]phenoxy]phenyl]- (9CI) (CA INDEX NAME)



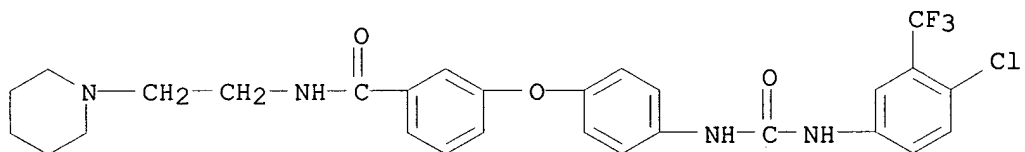
RN 284461-93-4 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



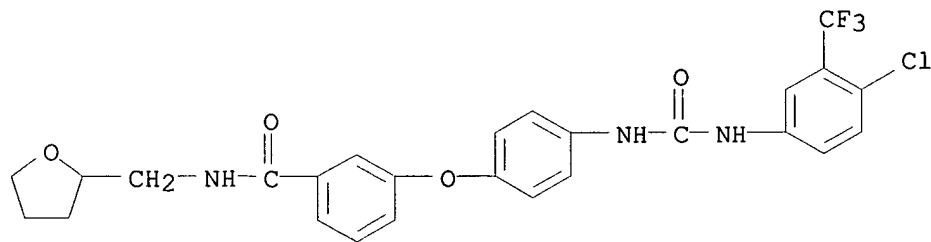
RN 284461-94-5 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



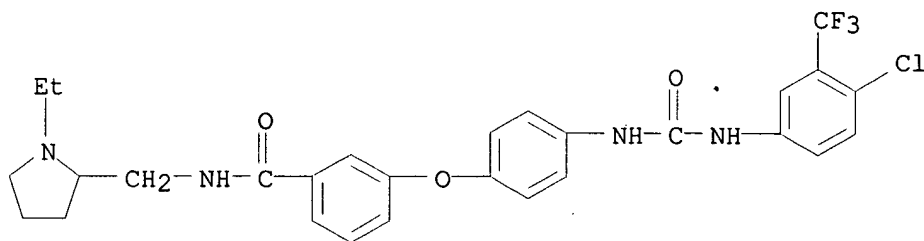
RN 284461-95-6 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



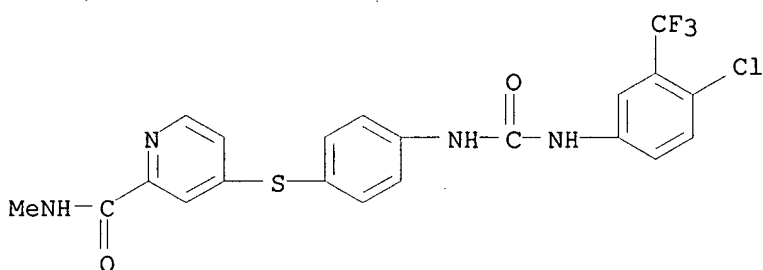
RN 284461-96-7 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[(1-ethyl-2-pyrrolidinyl)methyl]- (9CI) (CA INDEX NAME)



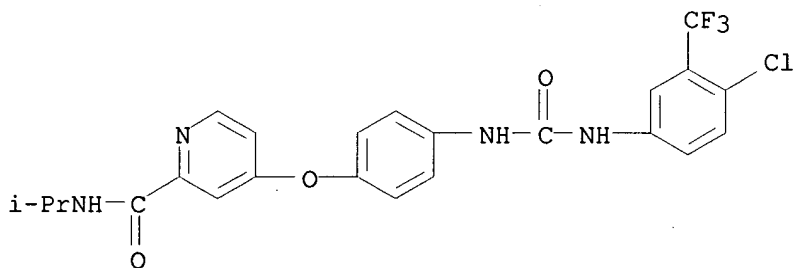
RN 284461-97-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



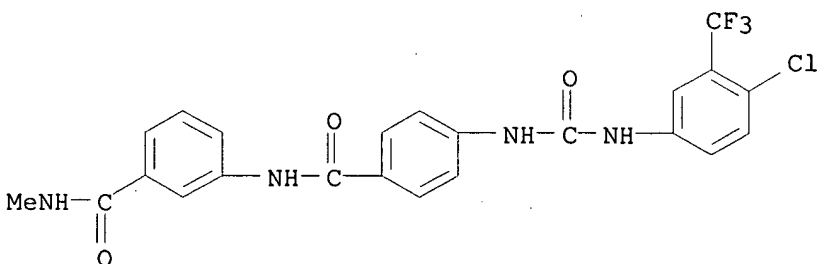
RN 284461-98-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



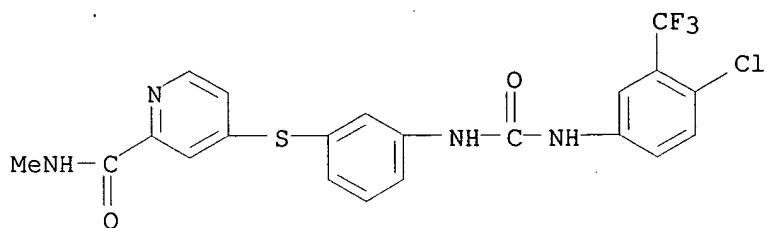
RN 284461-99-0 CAPLUS

CN Benzamide, 3-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]benzoyl]amino]-N-methyl- (9CI) (CA INDEX NAME)



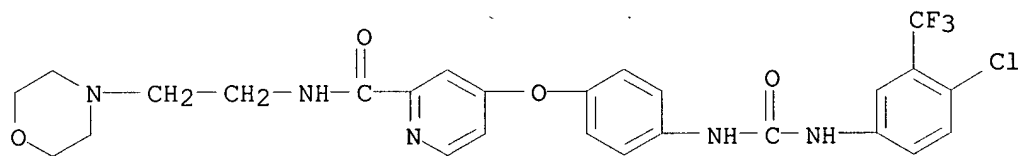
RN 284462-01-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



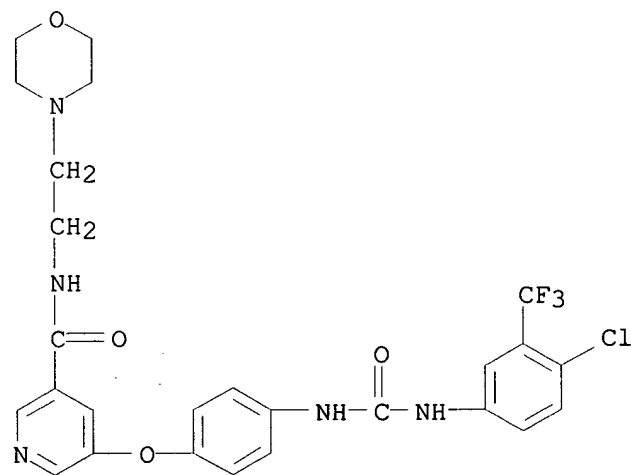
RN 284462-02-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



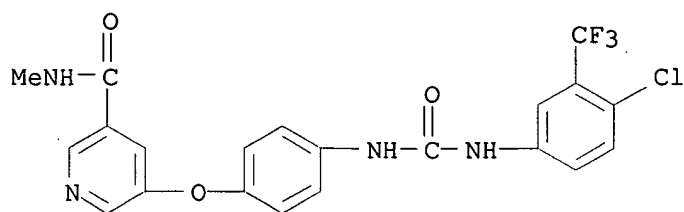
RN 284462-03-9 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



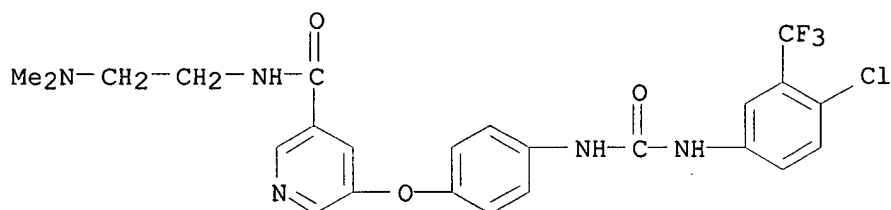
RN 284462-04-0 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



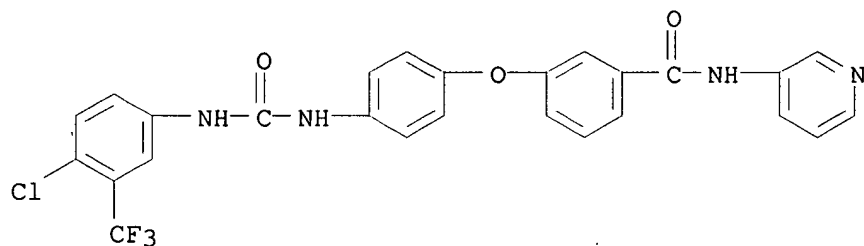
RN 284462-05-1 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



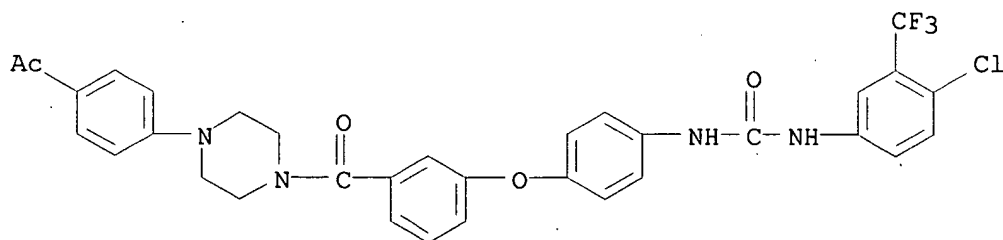
RN 284462-07-3 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-3-pyridinyl- (9CI) (CA INDEX NAME)



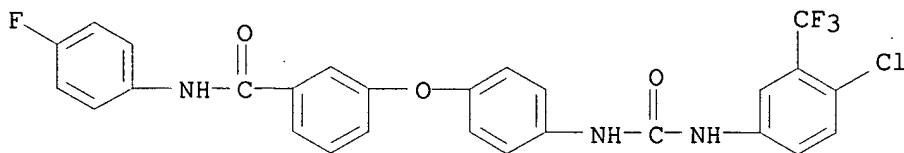
RN 284462-08-4 CAPLUS

CN Piperazine, 1-(4-acetylphenyl)-4-[3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]benzoyl]- (9CI) (CA INDEX NAME)



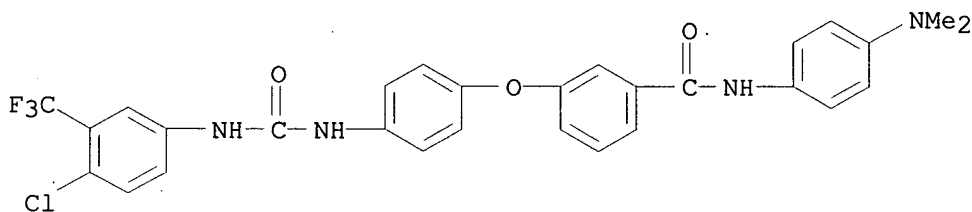
RN 284462-09-5 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



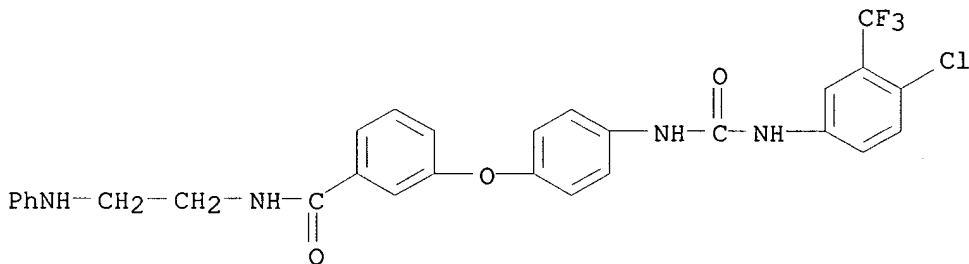
RN 284462-10-8 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]-N-[4-(dimethylamino)phenyl]- (9CI) (CA INDEX NAME)



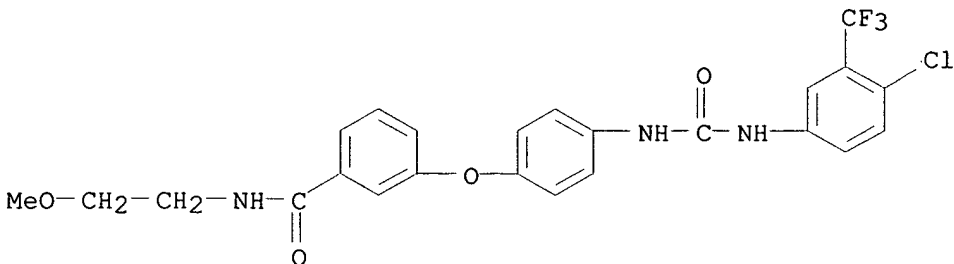
RN 284462-11-9 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]-N-[2-(phenylamino)ethyl]- (9CI) (CA INDEX NAME)



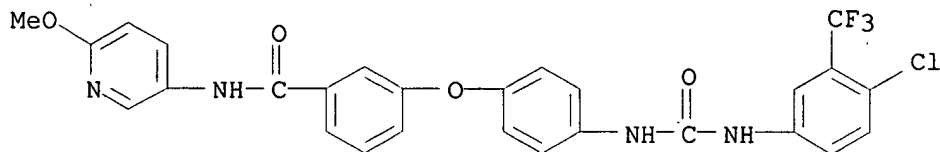
RN 284462-12-0 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]-N-(2-methoxyethyl)- (9CI) (CA INDEX NAME)



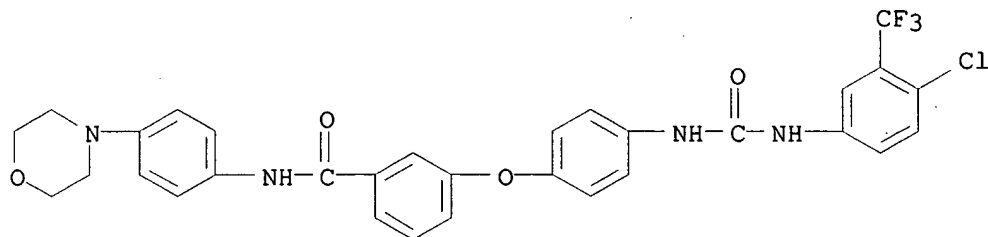
RN 284462-13-1 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]-N-(6-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



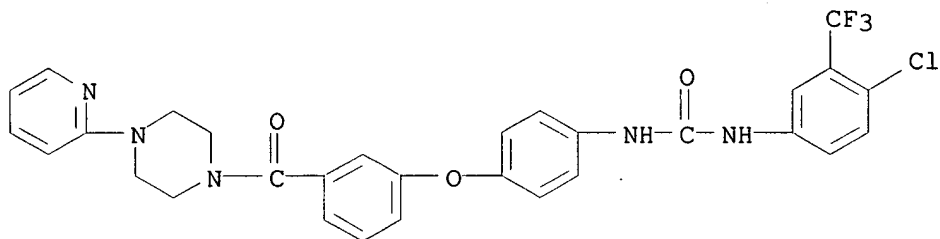
RN 284462-15-3 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



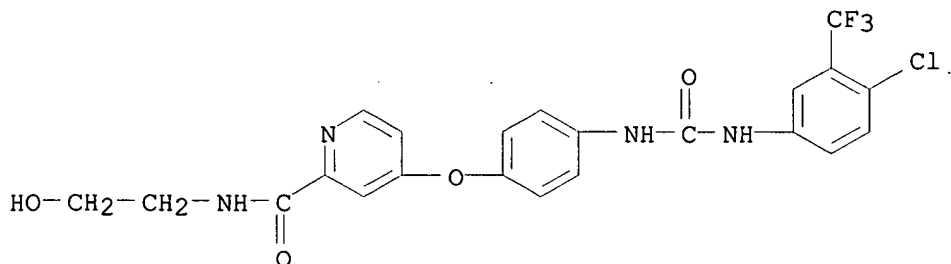
RN 284462-16-4 CAPLUS

CN Piperazine, 1-[3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]benzoyl]-4-(2-pyridinyl)- (9CI) (CA INDEX NAME)



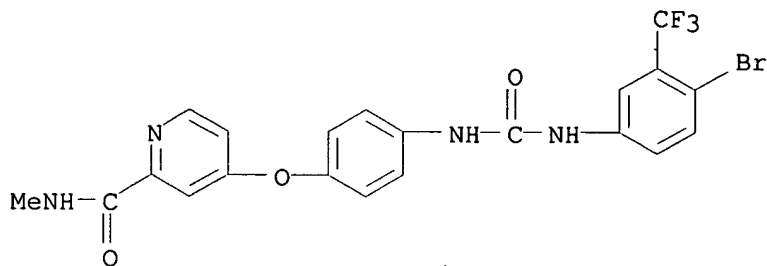
RN 284462-17-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

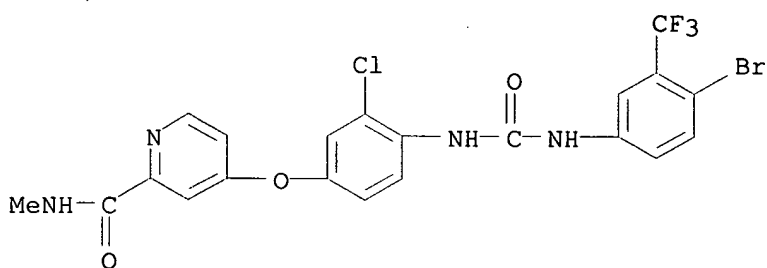


RN 284462-18-6 CAPLUS

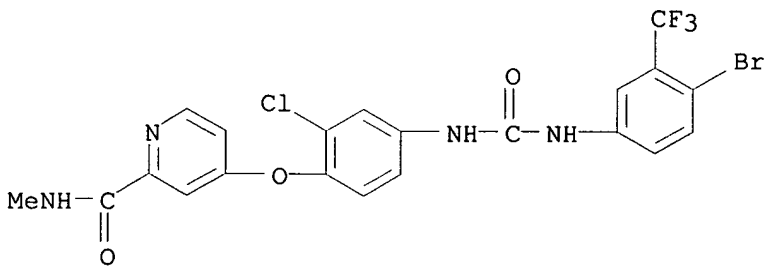
CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



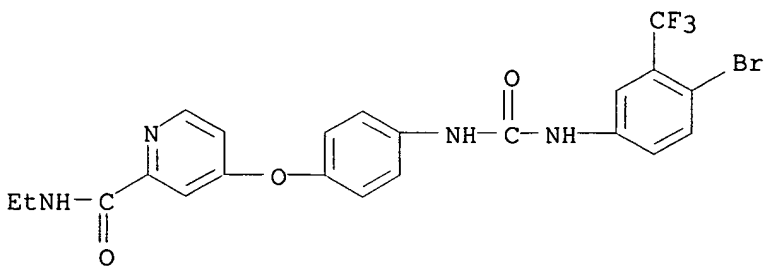
RN 284462-19-7 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-3-chlorophenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-20-0 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-chlorophenoxy]-N-methyl- (9CI) (CA INDEX NAME)



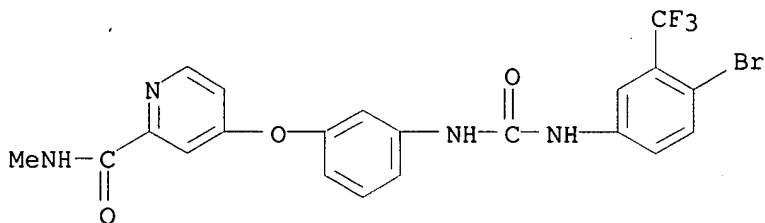
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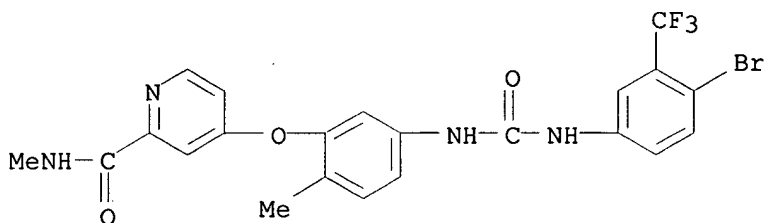
RN 284462-22-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



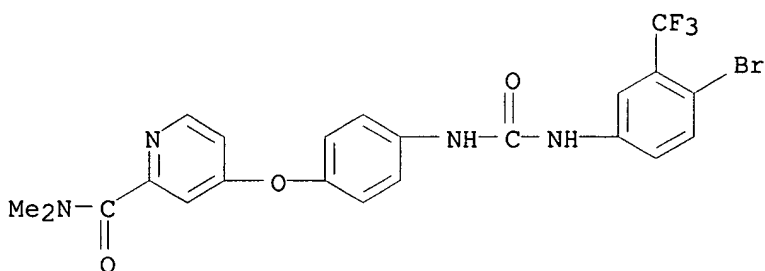
RN 284462-23-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



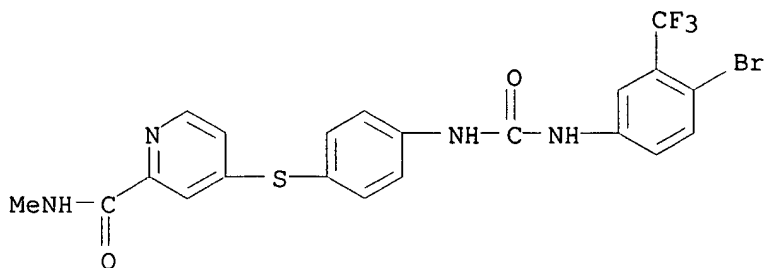
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CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



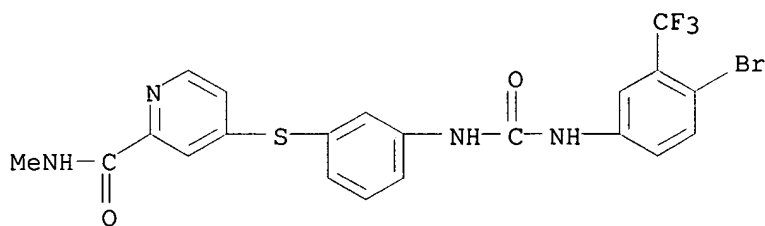
RN 284462-25-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



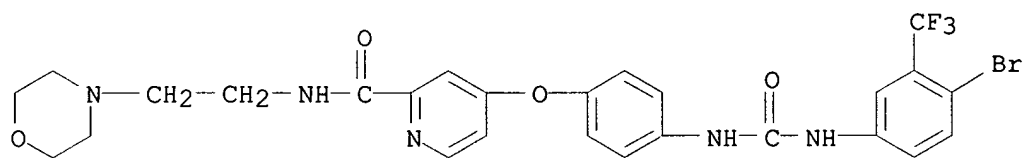
RN 284462-26-6 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



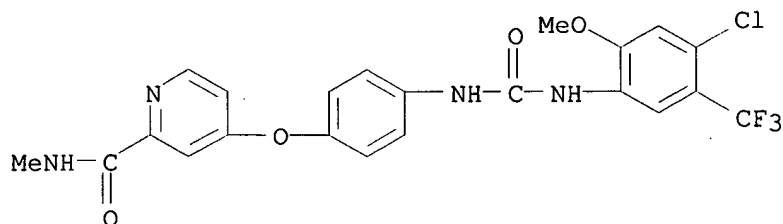
RN 284462-27-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



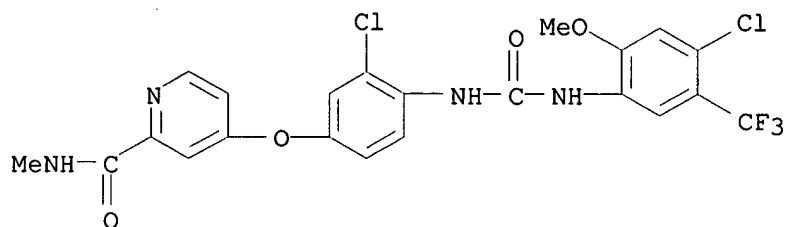
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CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



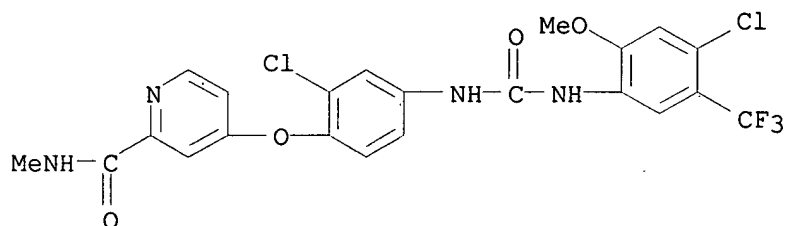
RN 284462-29-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-chloro-4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



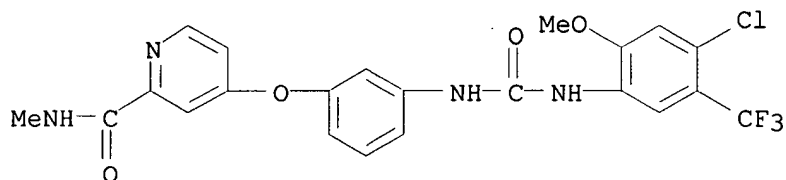
RN 284462-30-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[2-chloro-4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



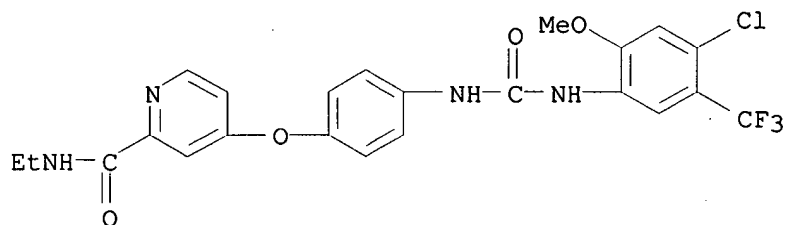
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CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



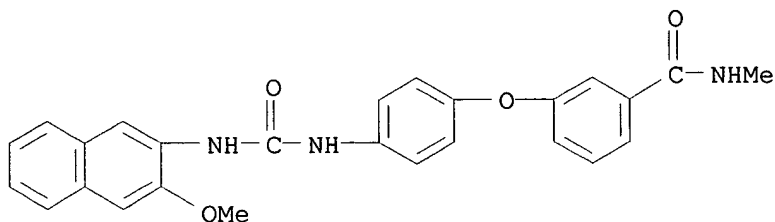
RN 284462-32-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-ethyl- (9CI) (CA INDEX NAME)



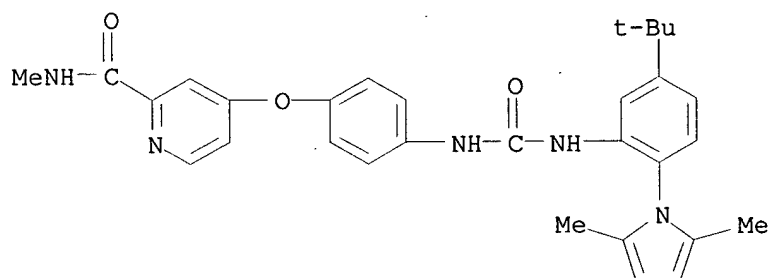
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CN Benzamide, 3-[4-[[[3-methoxy-2-naphthalenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



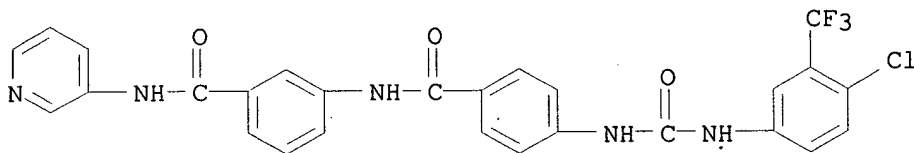
RN 284462-35-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[5-(1,1-dimethylethyl)-2-(2,5-dimethyl-1H-pyrrol-1-yl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



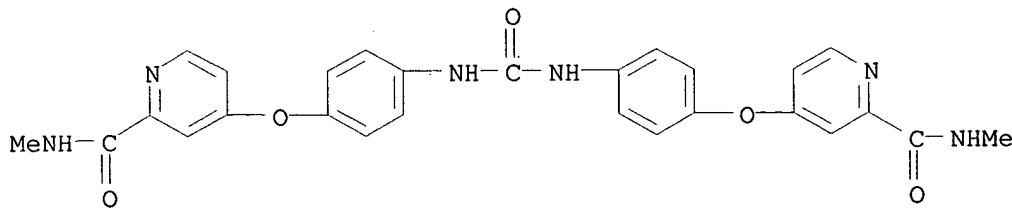
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CN Benzamide, 3-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]benzoyl]amino]-N-3-pyridinyl- (9CI) (CA INDEX NAME)



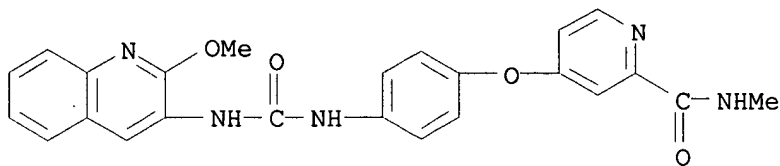
RN 284670-98-0 CAPLUS

CN 2-Pyridinecarboxamide, 4,4'-[carbonylbis(imino-4,1-phenyleneoxy)]bis[N-methyl- (9CI) (CA INDEX NAME)]



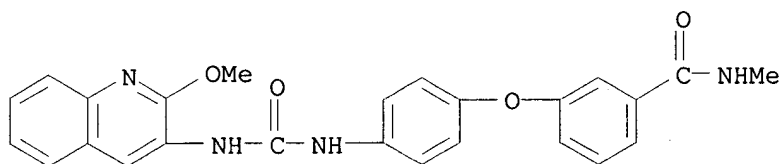
RN 432050-22-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-3-quinolinyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



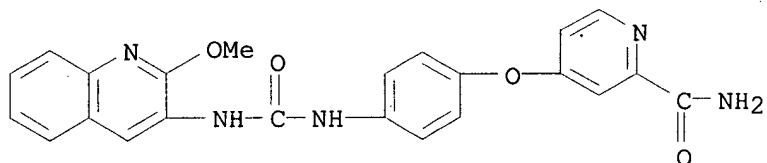
RN 432050-23-2 CAPLUS

CN Benzamide, 3-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



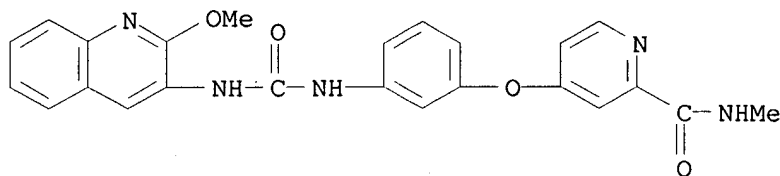
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CN 2-Pyridinecarboxamide, 4-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



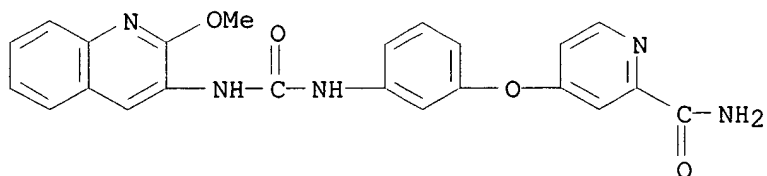
RN 432050-25-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 432050-26-5 CAPLUS

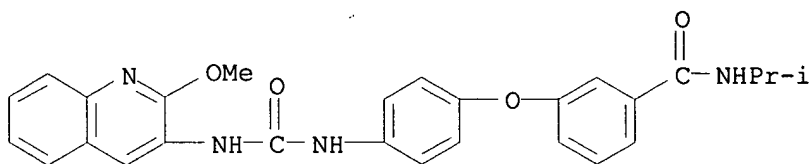
CN 2-Pyridinecarboxamide, 4-[3-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



RN 432050-27-6 CAPLUS

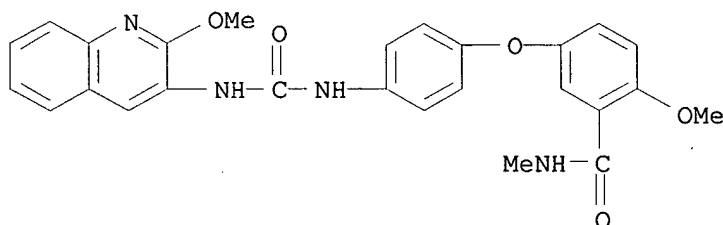
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(1-methylethyl)- (9CI) (CA INDEX NAME)



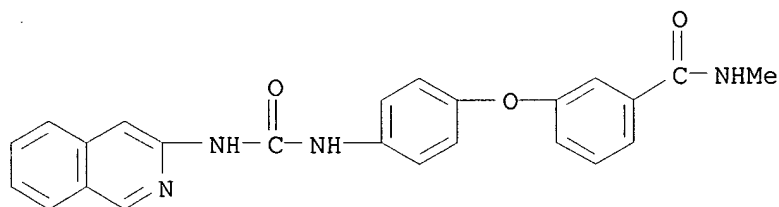
RN 432050-28-7 CAPLUS

CN Benzamide, 2-methoxy-5-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



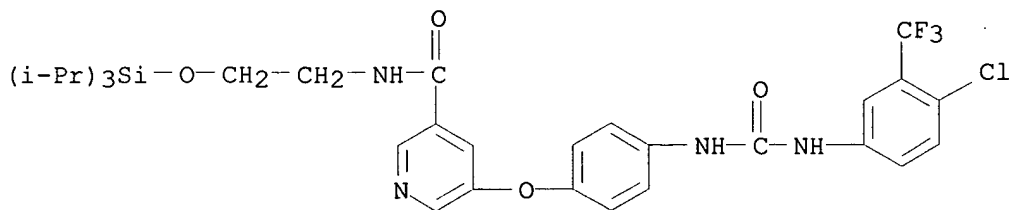
RN 432050-52-7 CAPLUS

CN Benzamide, 3-[4-[[[(3-isoquinolinylamino)carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



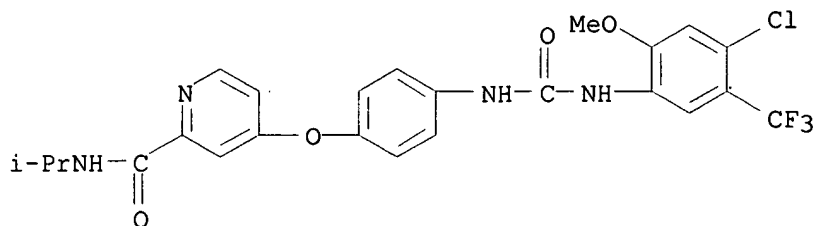
RN 447457-08-1 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-[[tris(1-methylethyl)silyl]oxy]ethyl]- (9CI) (CA INDEX NAME)



RN 447457-09-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

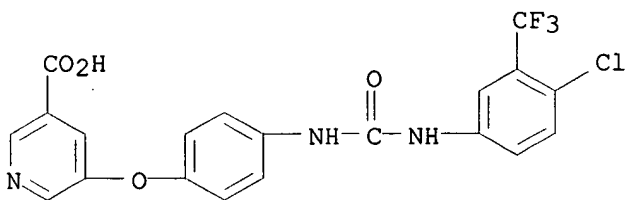


## IT 284462-71-1

RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)

RN 284462-71-1 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)

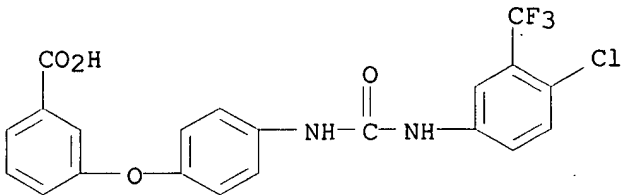


## IT 284462-69-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)

RN 284462-69-7 CAPLUS

CN Benzoic acid, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



L122 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:850357 CAPLUS

DOCUMENT NUMBER: 137:352907

TITLE: Preparation of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf kinase for the treatment of tumors and/or cancerous cell growth

INVENTOR(S): Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Robert, Sibley N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 63 pp., Cont.-in-part of U.S. Ser. No. 758,548.

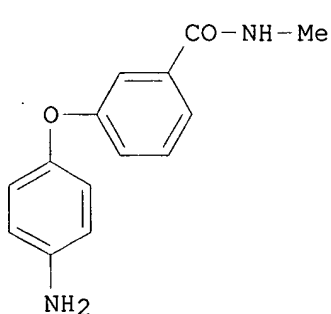
DOCUMENT TYPE: CODEN: USXXCO  
LANGUAGE: Patent  
FAMILY ACC. NUM. COUNT: 5 English  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002165394	A1	20021107	US 2001-777920	20010207
ZA 2001005751	A	20030714	ZA 2001-5751	20010712
US 2002137774	A1	20020926	US 2001-907970	20010719
WO 2002062763	A2	20020815	WO 2002-US3361	20020207
WO 2002062763	A3	20021010		

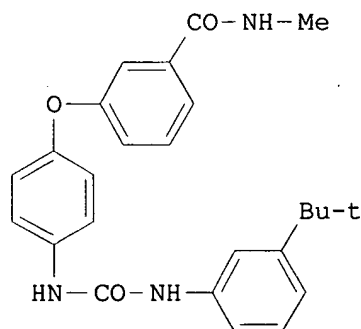
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US 2003139605 A1 20030724 US 2002-71248 20020211  
PRIORITY APPLN. INFO.: US 1999-115877P P 19990113  
US 1999-257266 B2 19990225  
US 1999-425228 B2 19991022  
US 2001-758548 A2 20010112  
US 1999-115878P P 19990113  
US 2001-777920 A 20010207  
US 2001-948915 A1 20010910

OTHER SOURCE(S): MARPAT 137:352907  
ED Entered STN: 08 Nov 2002  
GI



II



III

AB Title compds. B-NHCONH-L-(M-L1)<sub>q</sub> (I) [B = (un)substituted pyridyl, quinolinyl, isoquinolinyl; L = 5 or 6 membered cyclic structure; L1 = substituted cyclic moiety having at least 5 members; M = bridging group having at least one atom; q = 1-3; with proviso that L and L1 contain 0-4 hetero atoms, e.g., N, O and S] and their pharmaceutically acceptable salts were prepd. For example, coupling of aniline II, e.g., prepd. from Et 3-hydroxybenzoate in 4-steps, with bis(trichloromethyl)carbonate followed by 3-tert-butylaniline afforded urea III. In in vitro raf kinase assays, 112-specific examples of compds. I inhibited kinase activity with IC<sub>50</sub> values ranging from 10 nM-10 .mu.M. Compds. I are useful for the



IT treatment of cancerous cell growth mediated by raf kinase.

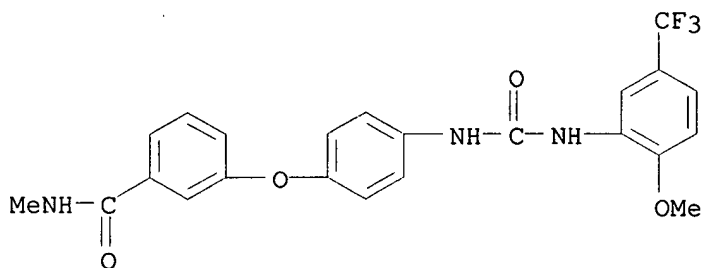
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(drug candidate; prepn. of quinolyl, isoquinolyl or pyridyl-ureas as  
inhibitors of raf kinase)

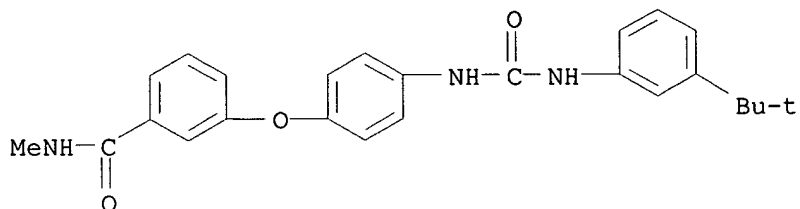
RN 228418-48-2 CAPLUS

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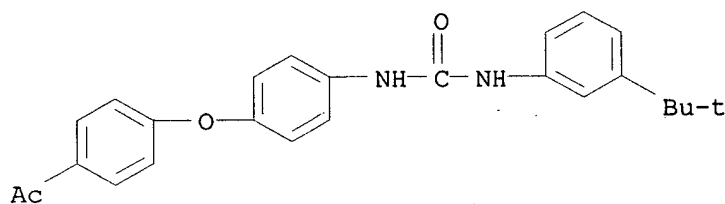


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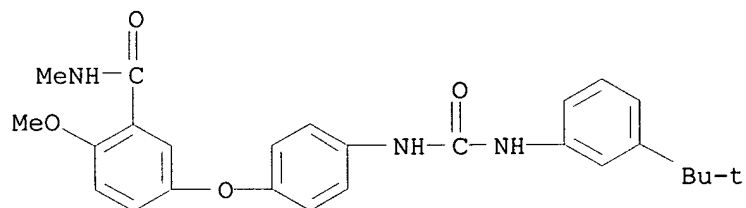


RN 284461-34-3 CAPLUS

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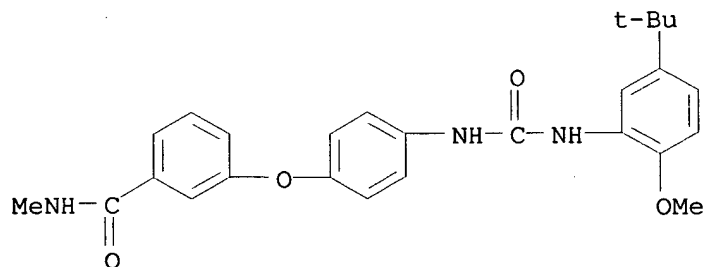
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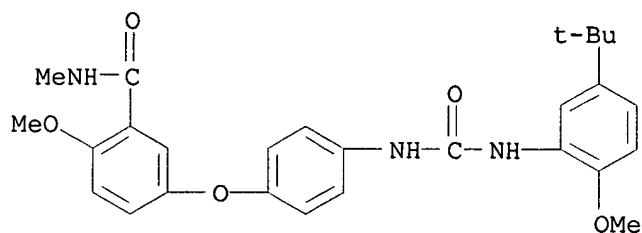
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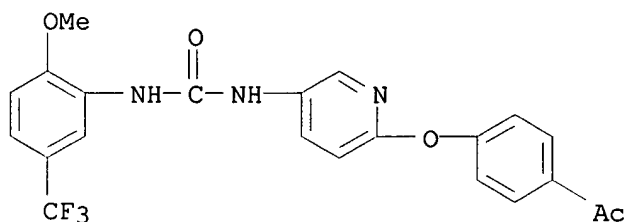
RN 284461-37-6 CAPLUS

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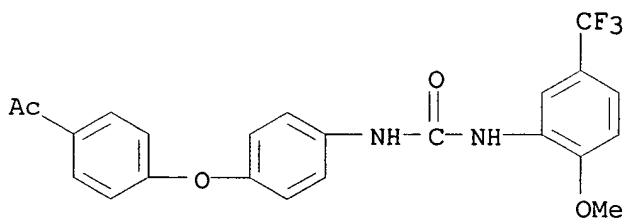
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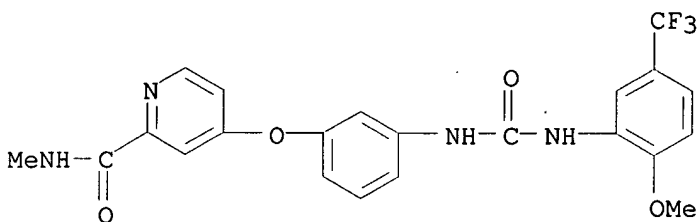
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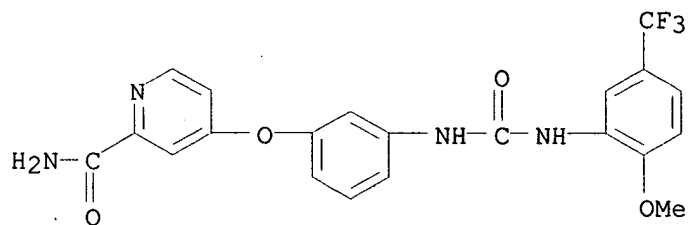
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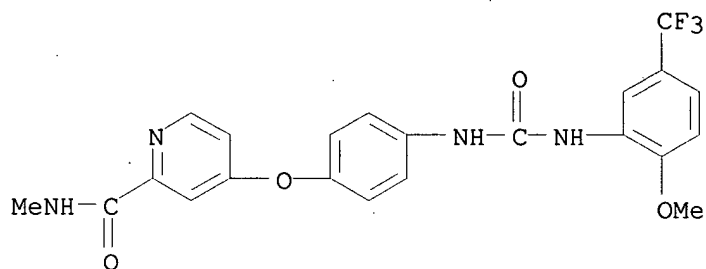
RN 284461-43-4 CAPLUS

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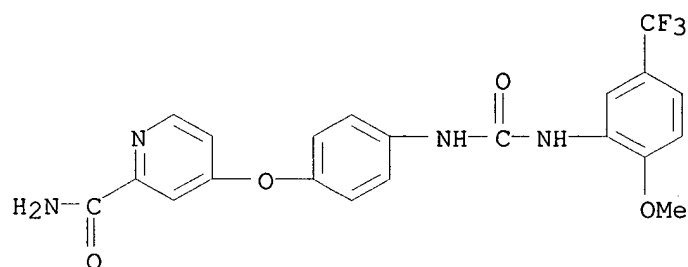
RN 284461-44-5 CAPLUS

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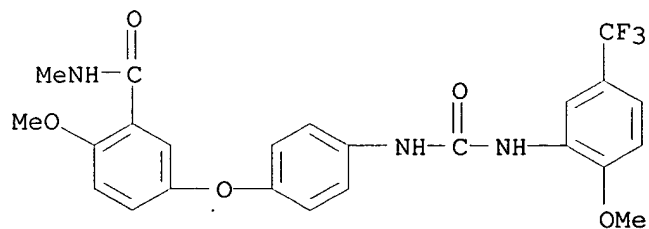
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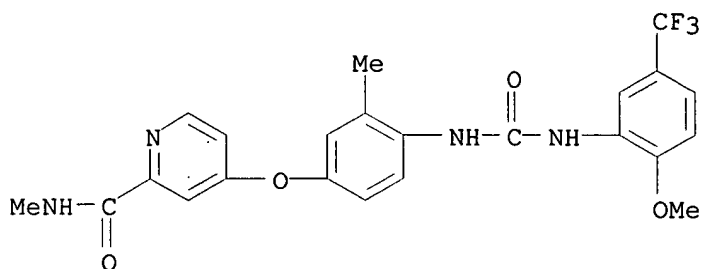
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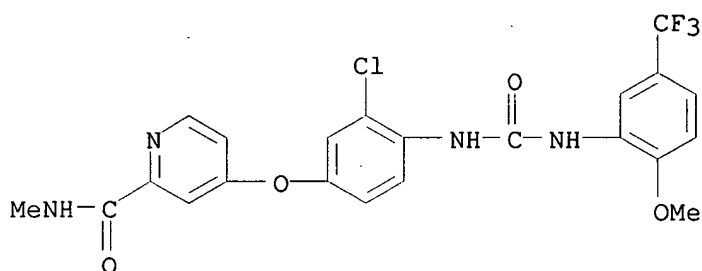


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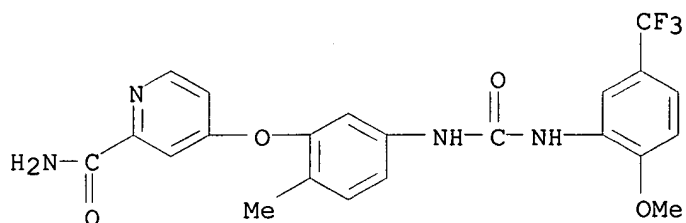
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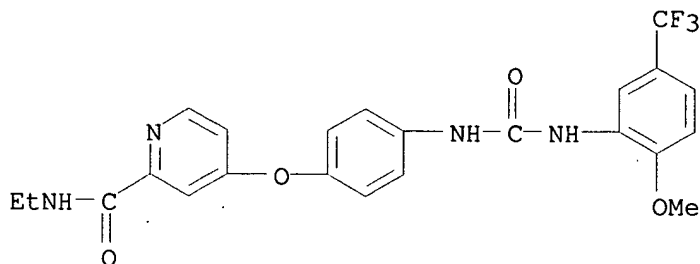
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RN 284461-49-0 CAPLUS  
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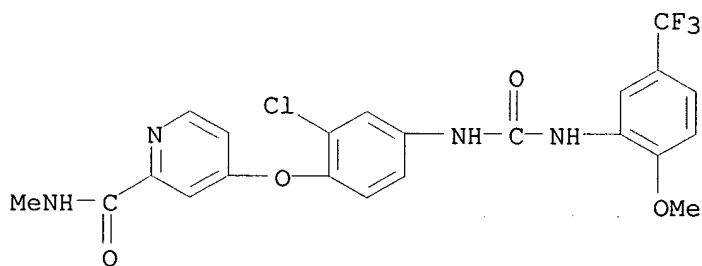


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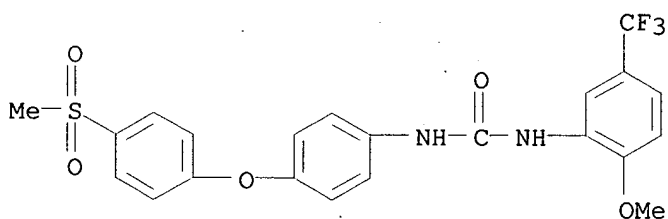
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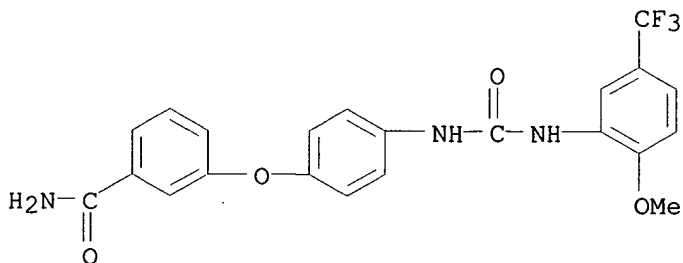
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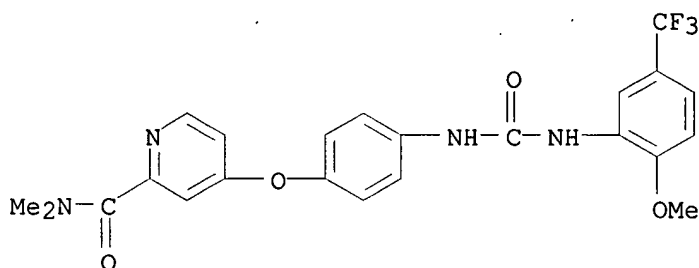


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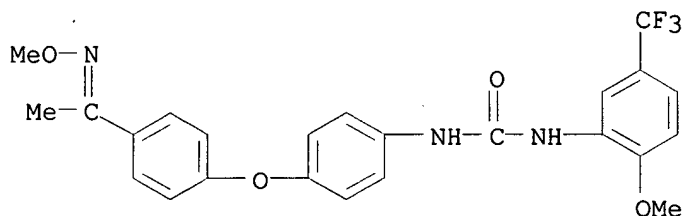
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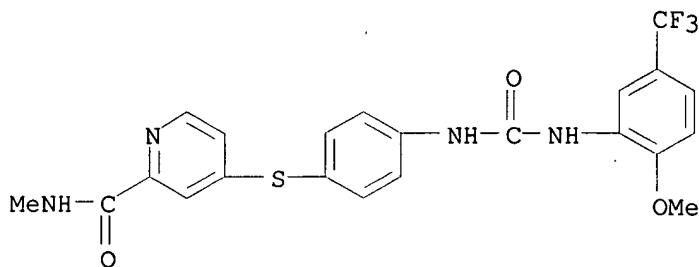
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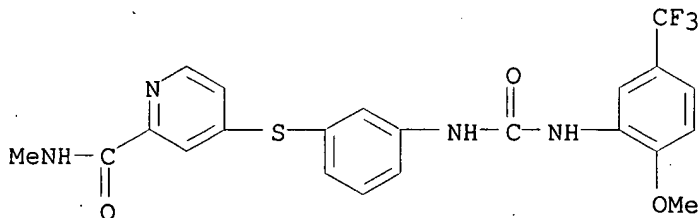
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RN 284461-58-1 CAPLUS  
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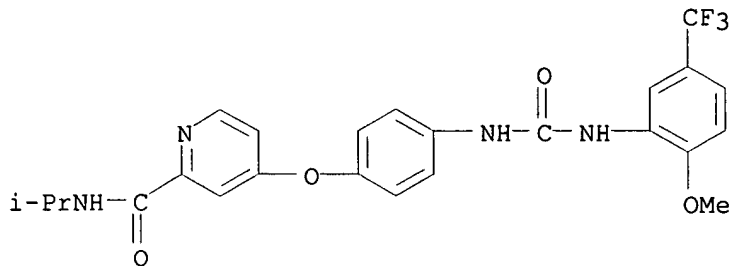


RN 284461-60-5 CAPLUS  
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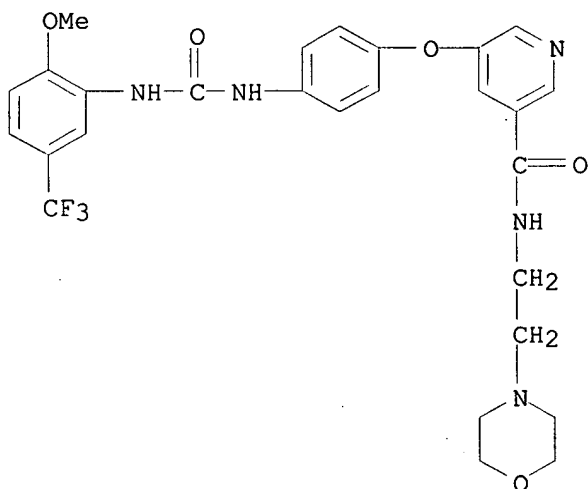
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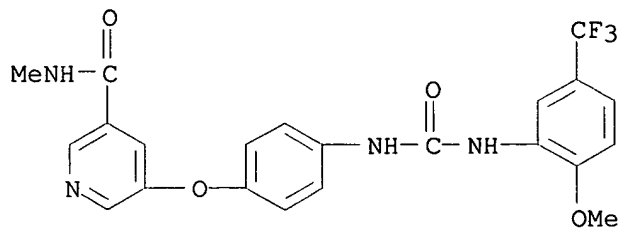
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RN 284461-63-8 CAPLUS

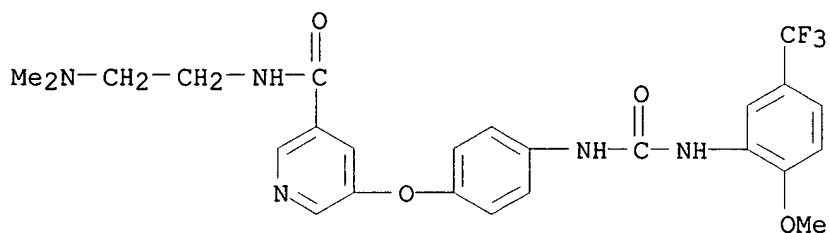
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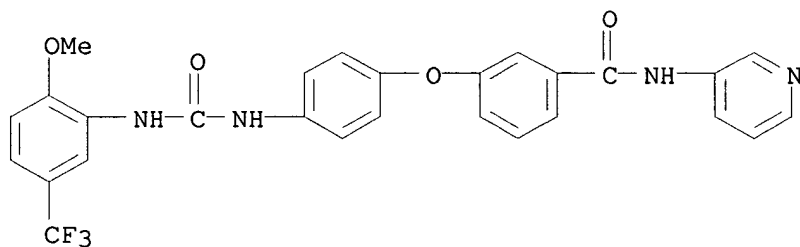
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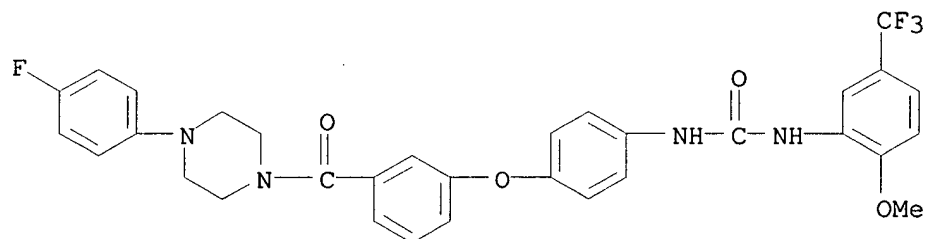
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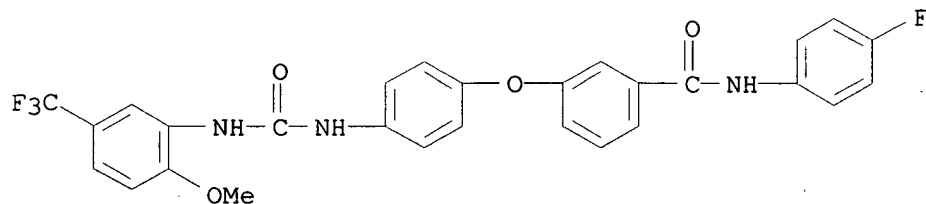
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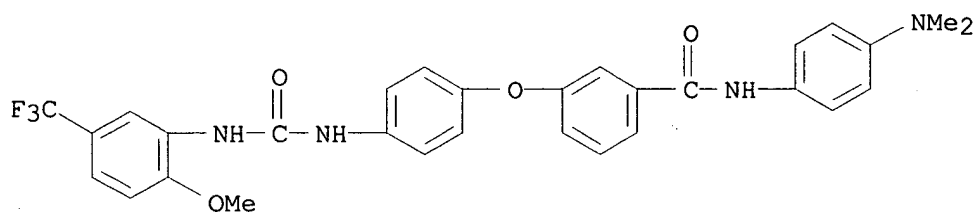
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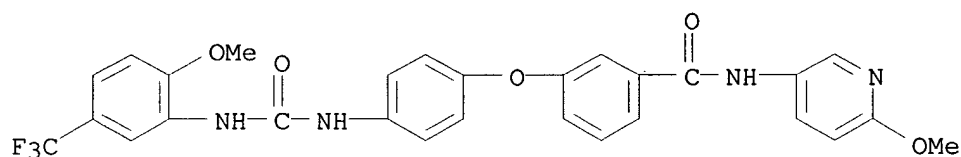
RN 284461-68-3 CAPLUS

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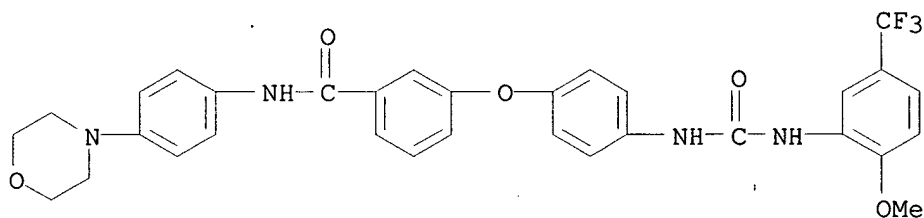
RN 284461-69-4 CAPLUS

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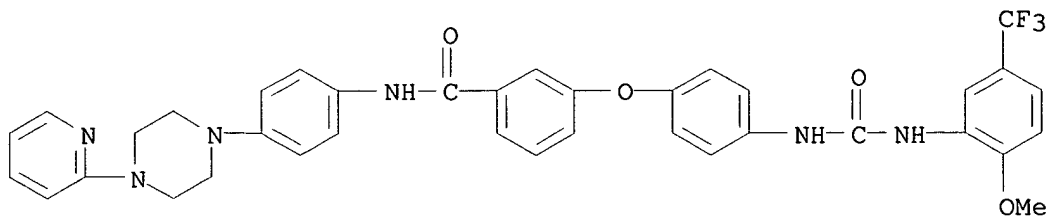
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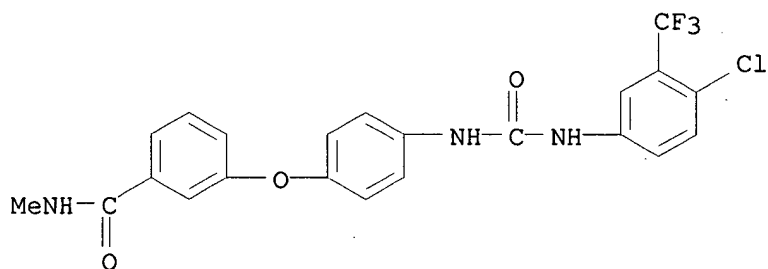
RN 284461-71-8 CAPLUS

CN Benzamide, 3-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-[4-(2-pyridinyl)-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



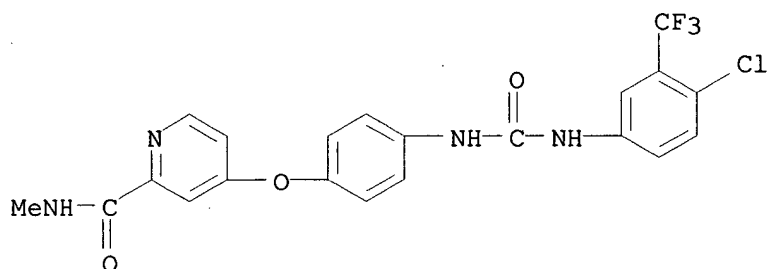
RN 284461-72-9 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



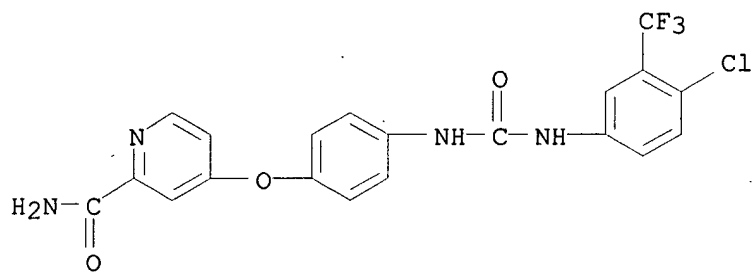
RN 284461-73-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



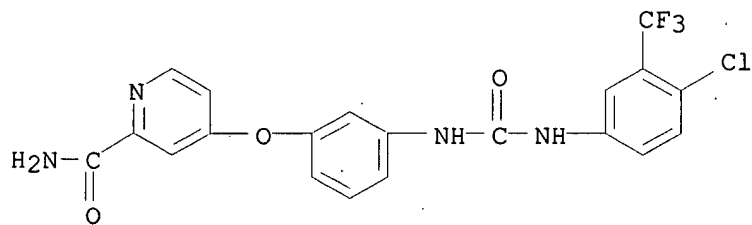
RN 284461-74-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



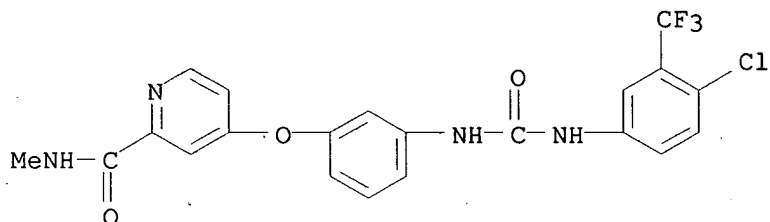
RN 284461-75-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



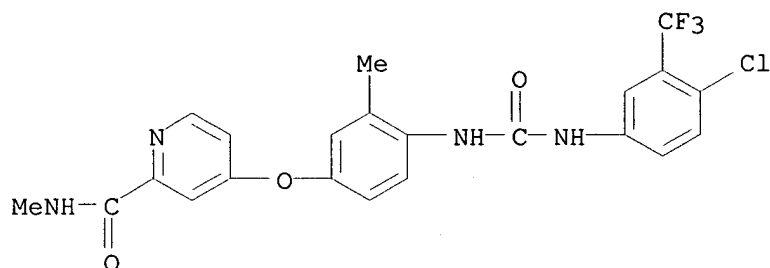
RN 284461-76-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



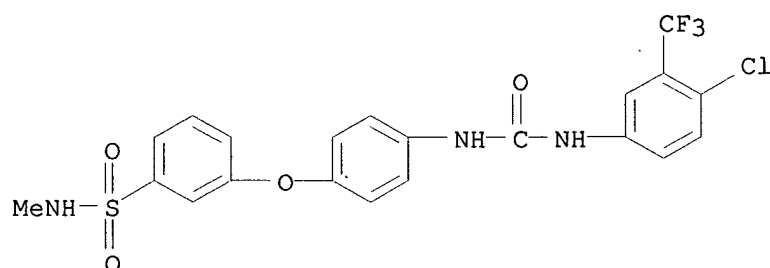
RN 284461-78-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-3-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



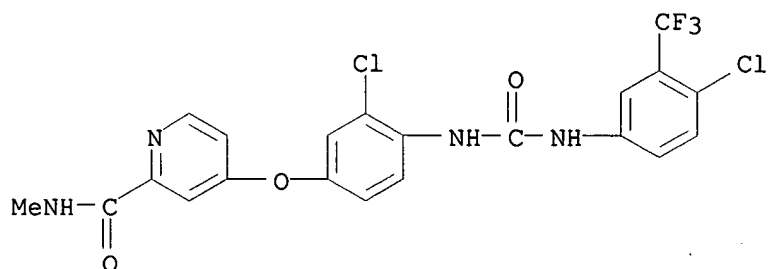
RN 284461-79-6 CAPLUS

CN Benzenesulfonamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



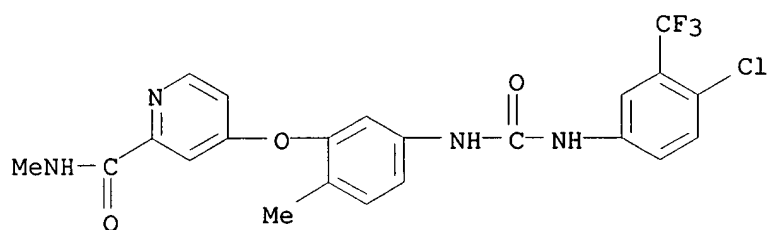
RN 284461-80-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-chloro-4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



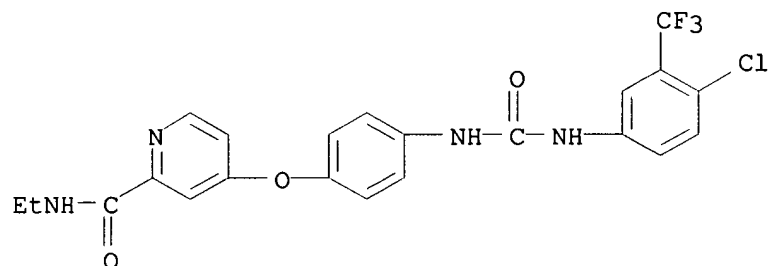
RN 284461-81-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



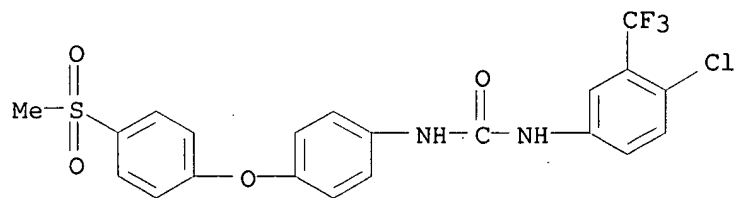
RN 284461-82-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-ethyl- (9CI) (CA INDEX NAME)



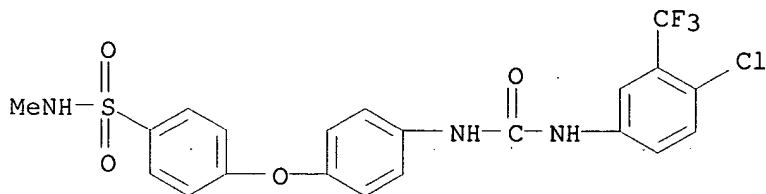
RN 284461-84-3 CAPLUS

CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[4-(methylsulfonyl)phenoxy]phenyl]- (9CI) (CA INDEX NAME)



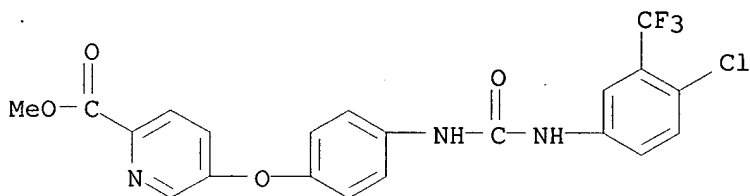
RN 284461-85-4 CAPLUS

CN Benzenesulfonamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



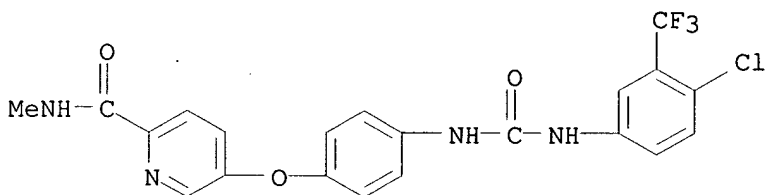
RN 284461-86-5 CAPLUS

CN 2-Pyridinecarboxylic acid, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, methyl ester (9CI)  
(CA INDEX NAME)



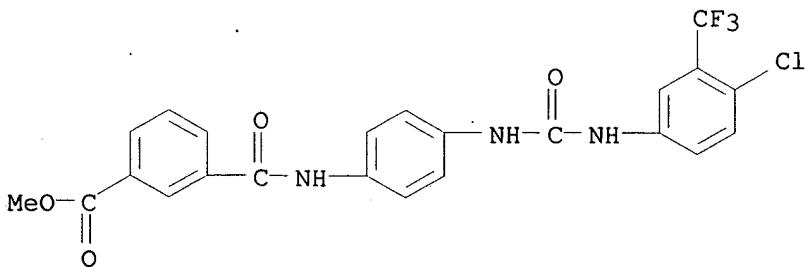
RN 284461-88-7 CAPLUS

CN 2-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



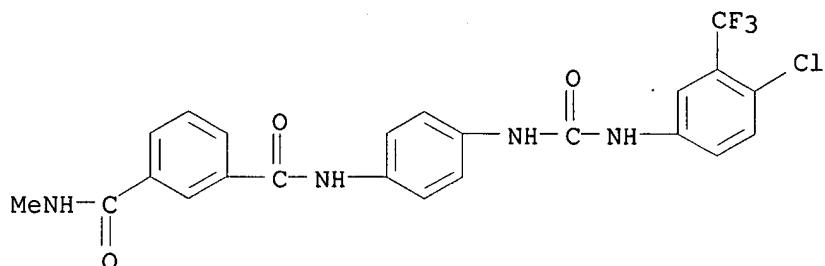
RN 284461-89-8 CAPLUS

CN Benzoic acid, 3-[[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



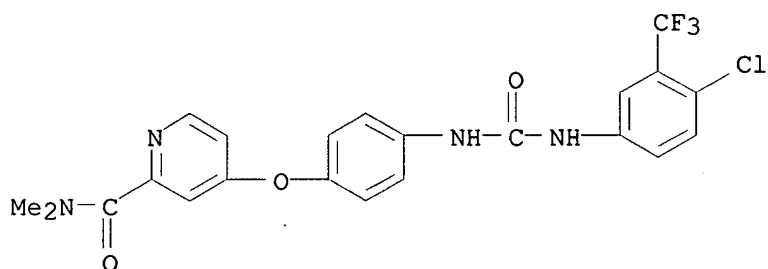
RN 284461-90-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]-N'-methyl- (9CI) (CA INDEX NAME)



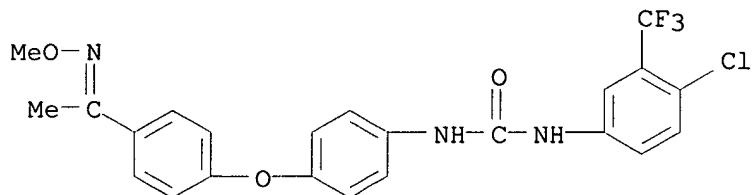
RN 284461-91-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



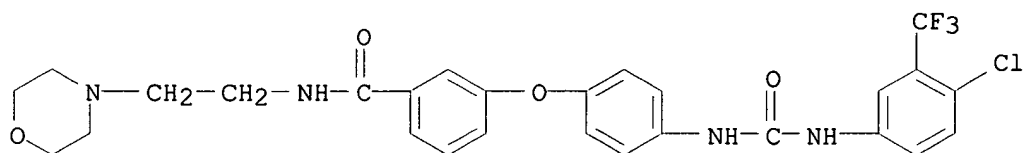
RN 284461-92-3 CAPLUS

CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[4-[1-(methoxyimino)ethyl]phenoxy]phenyl]- (9CI) (CA INDEX NAME)



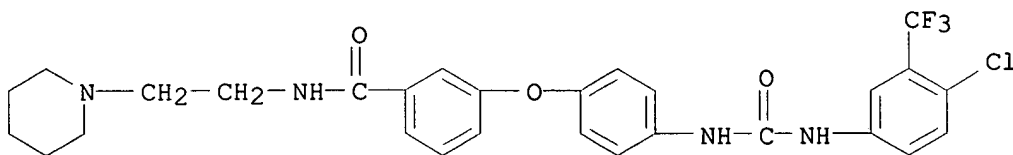
RN 284461-93-4 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



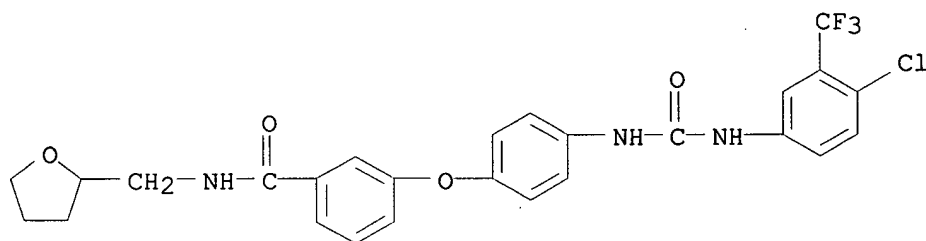
RN 284461-94-5 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



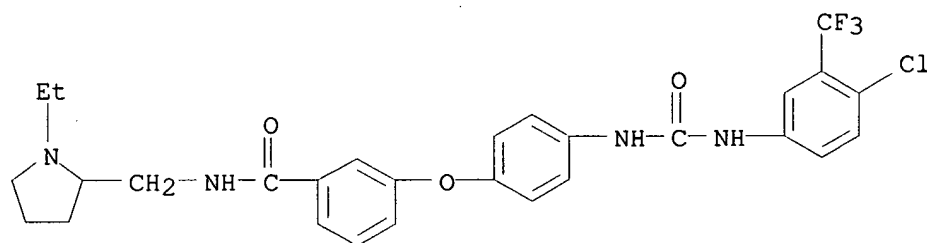
RN 284461-95-6 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



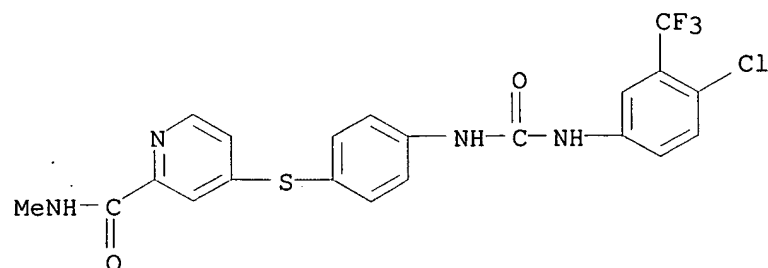
RN 284461-96-7 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[(1-ethyl-2-pyrrolidinyl)methyl]- (9CI) (CA INDEX NAME)



RN 284461-97-8 CAPLUS

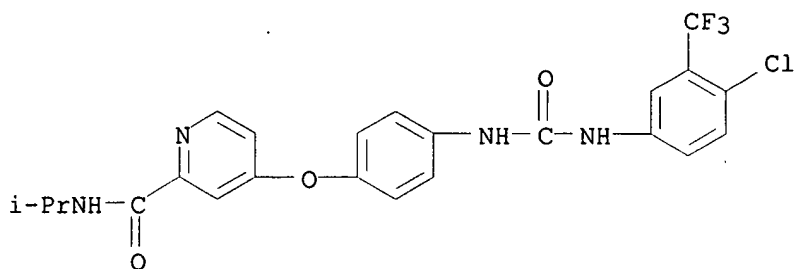
CN 2-Pyridinecarboxamide, 4-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-98-9 CAPLUS

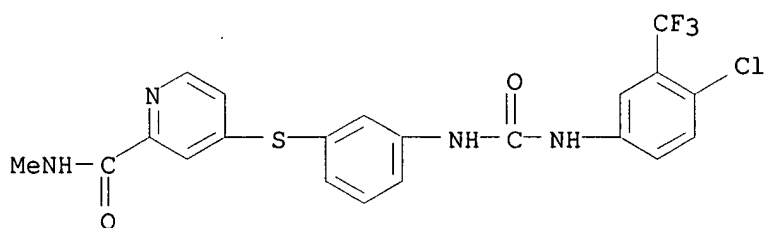
CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)





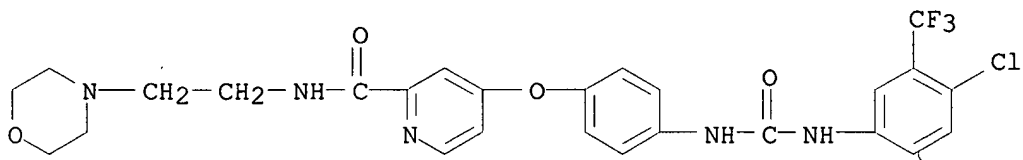
RN 284462-01-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



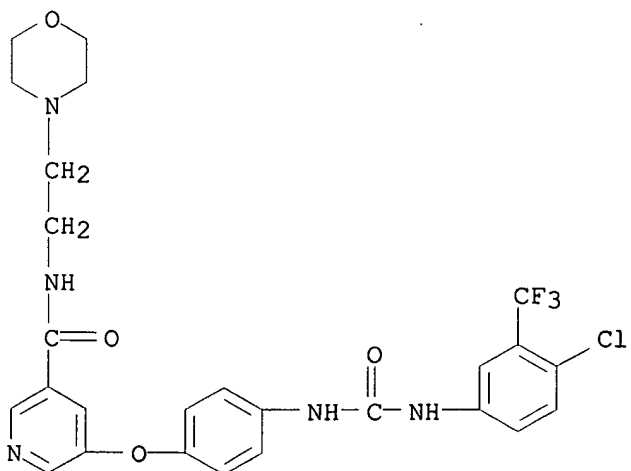
RN 284462-02-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



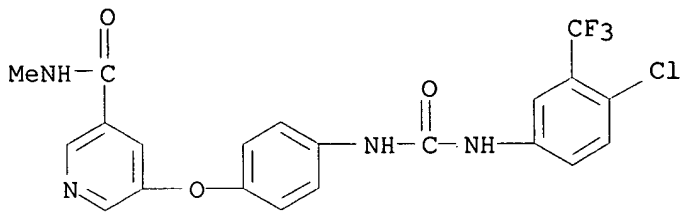
RN 284462-03-9 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



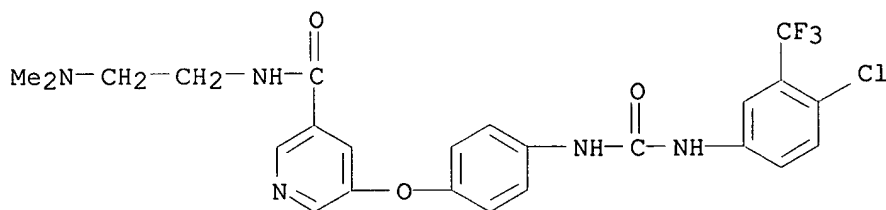
RN 284462-04-0 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



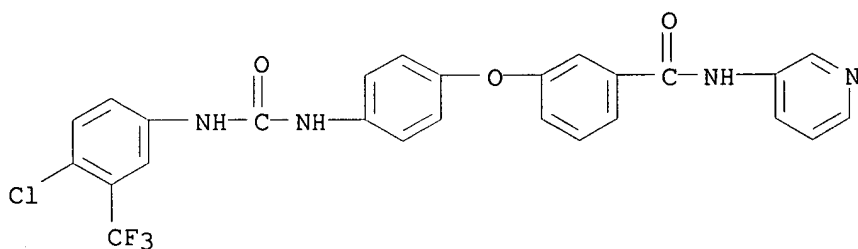
RN 284462-05-1 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



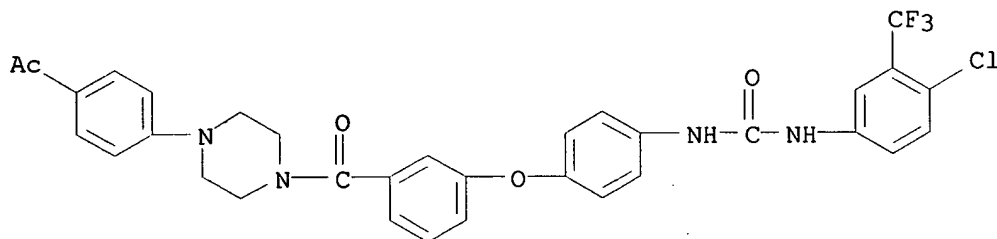
RN 284462-07-3 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-3-pyridinyl- (9CI) (CA INDEX NAME)



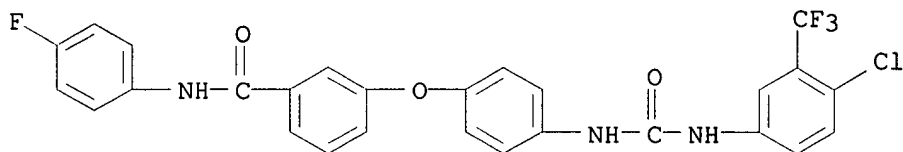
RN 284462-08-4 CAPLUS

CN Piperazine, 1-(4-acetylphenyl)-4-[3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]benzoyl]- (9CI) (CA INDEX NAME)



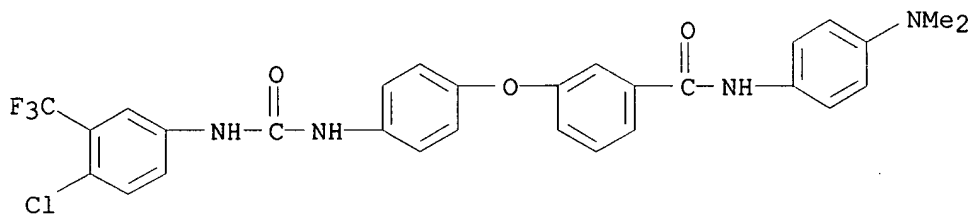
RN 284462-09-5 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



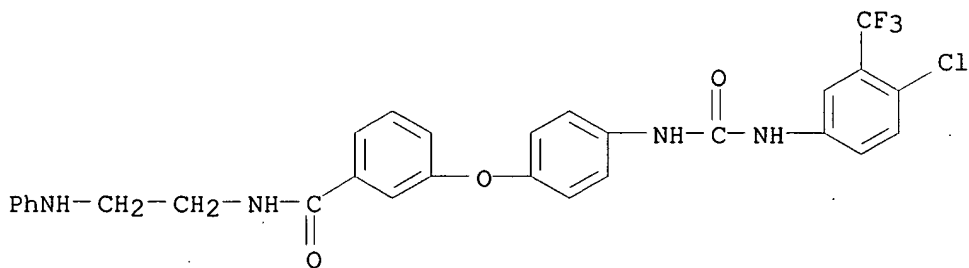
RN 284462-10-8 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-(dimethylamino)phenyl]- (9CI) (CA INDEX NAME)



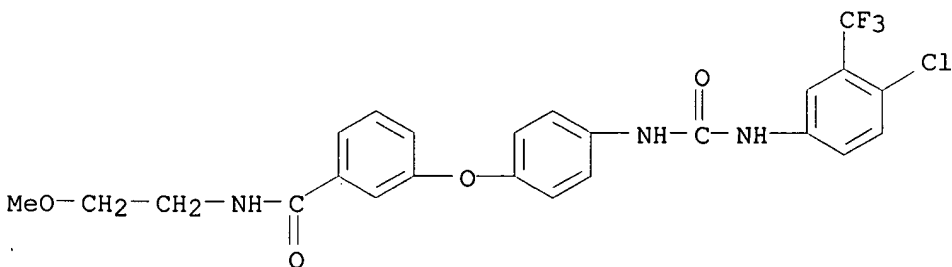
RN 284462-11-9 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(phenylamino)ethyl]- (9CI) (CA INDEX NAME)



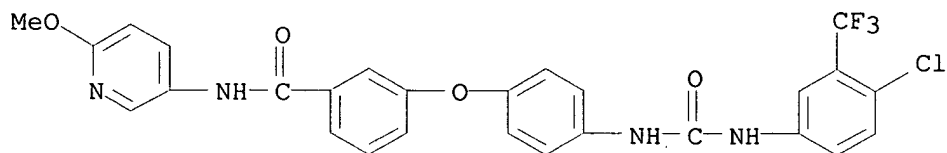
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CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(2-methoxyethyl)- (9CI) (CA INDEX NAME)



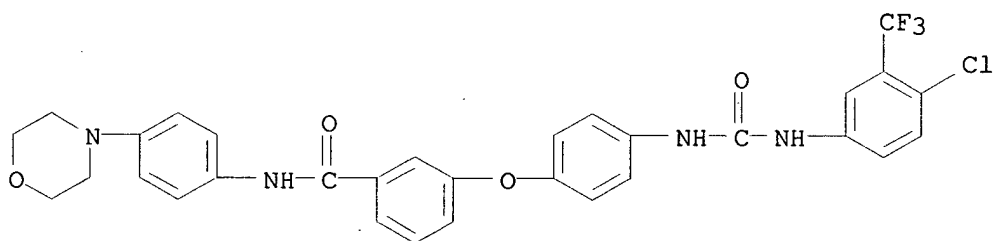
RN 284462-13-1 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(6-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



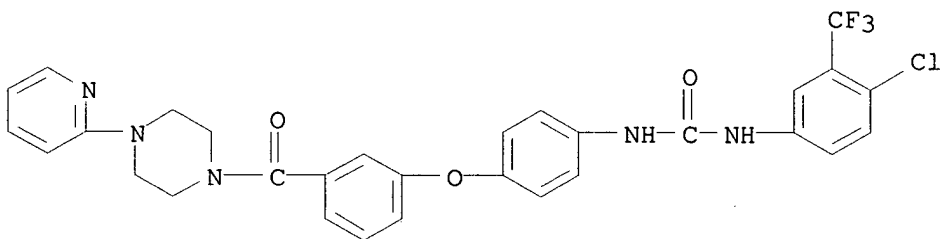
RN 284462-15-3 CAPLUS

CN Benzamide, 3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



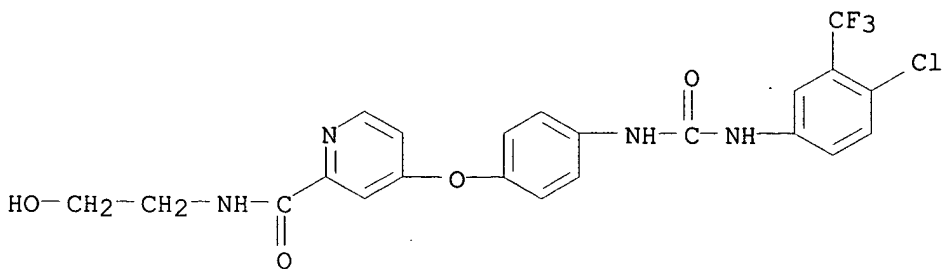
RN 284462-16-4 CAPLUS

CN Piperazine, 1-[3-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]benzoyl]-4-(2-pyridinyl)- (9CI) (CA INDEX NAME)



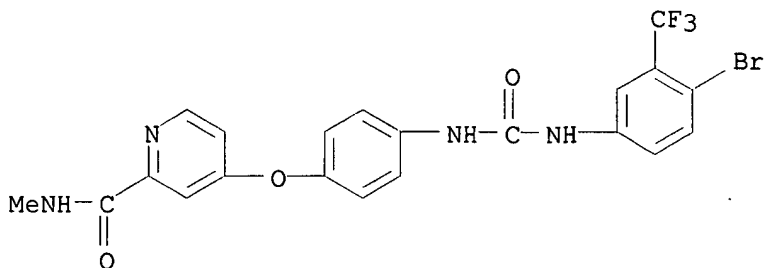
RN 284462-17-5 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



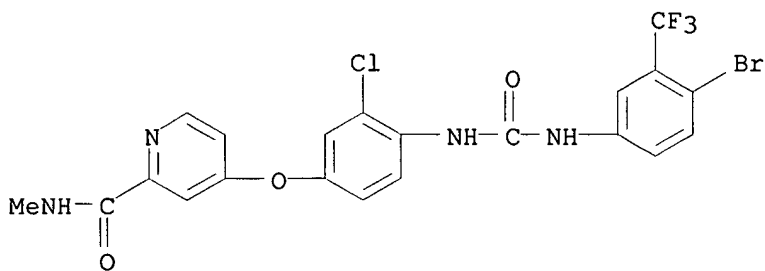
RN 284462-18-6 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



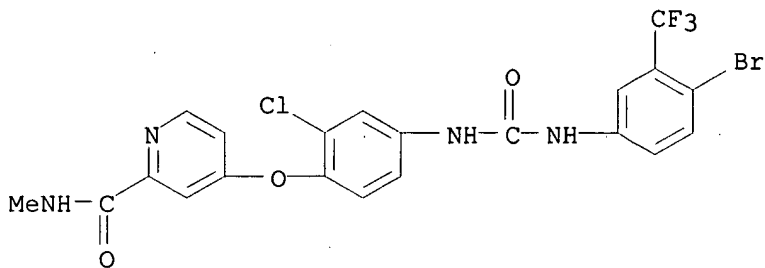
RN 284462-19-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-3-chlorophenoxy]-N-methyl- (9CI) (CA INDEX NAME)



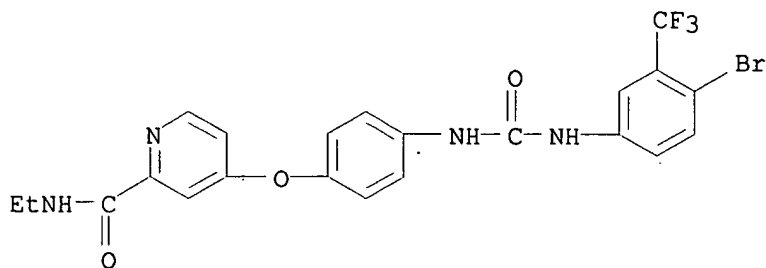
RN 284462-20-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-chlorophenoxy]-N-methyl- (9CI) (CA INDEX NAME)

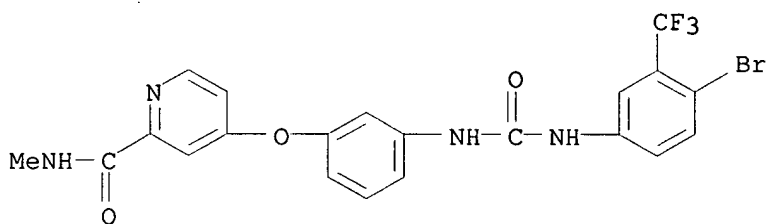


RN 284462-21-1 CAPLUS

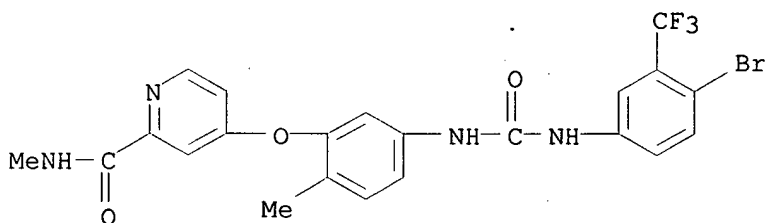
CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-ethyl- (9CI) (CA INDEX NAME)



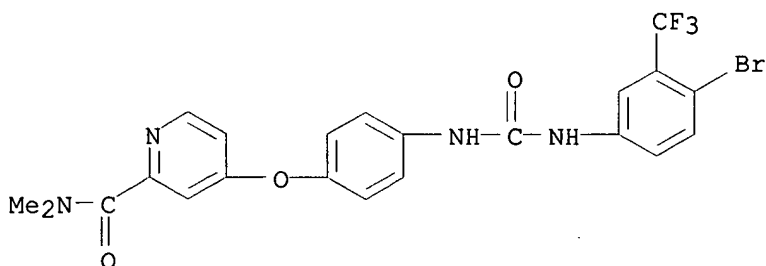
RN 284462-22-2 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



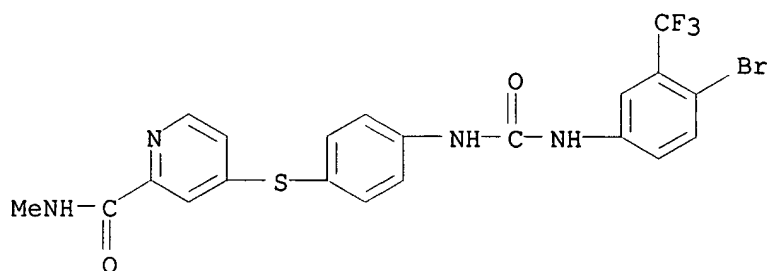
RN 284462-23-3 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-24-4 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)

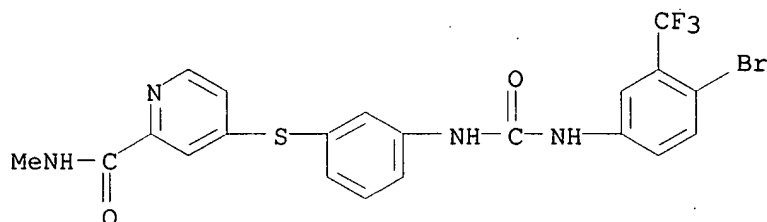


RN 284462-25-5 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenylthio]-N-methyl- (9CI) (CA INDEX NAME)



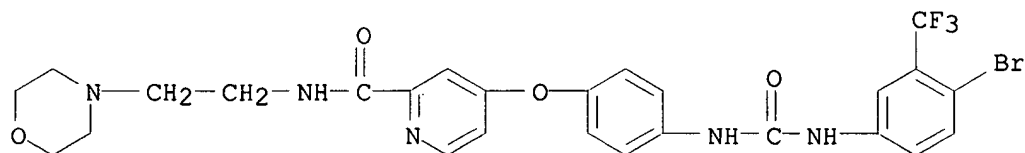
RN 284462-26-6 CAPLUS

CN 2-Pyridinecarboxamide, 4-[[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]thio]-N-methyl- (9CI) (CA INDEX NAME)



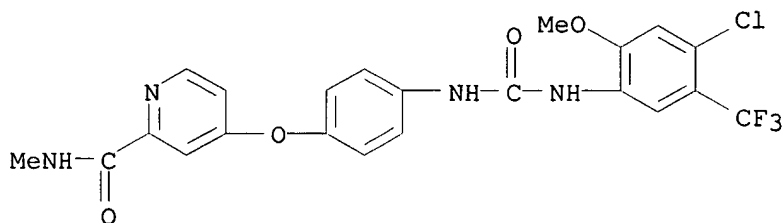
RN 284462-27-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



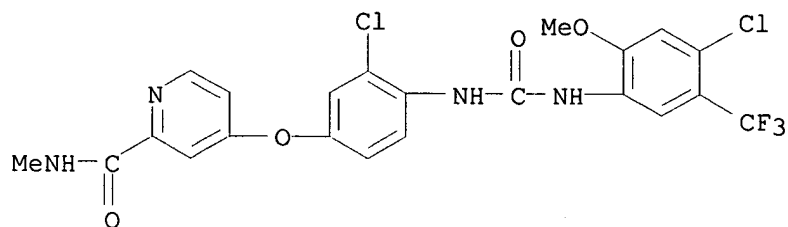
RN 284462-28-8 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



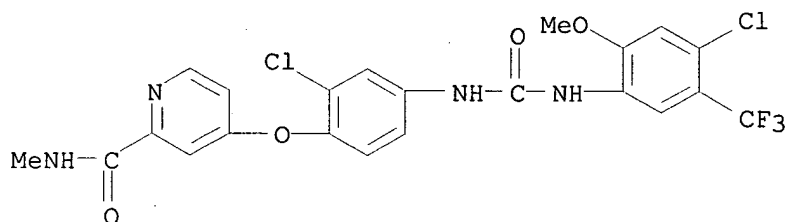
RN 284462-29-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-chloro-4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



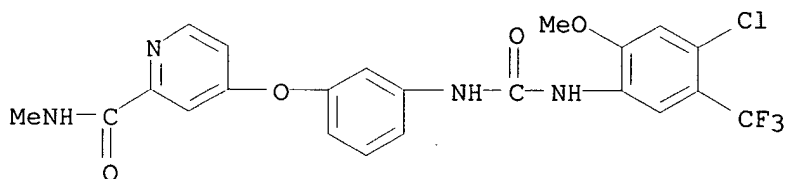
RN 284462-30-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[2-chloro-4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



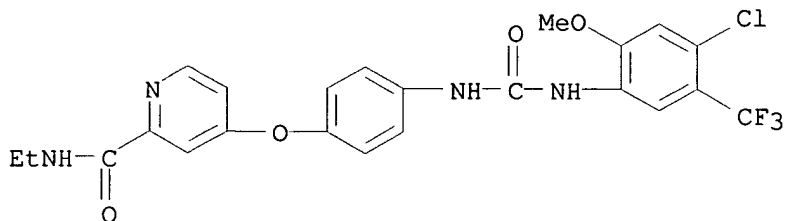
RN 284462-31-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-32-4 CAPLUS

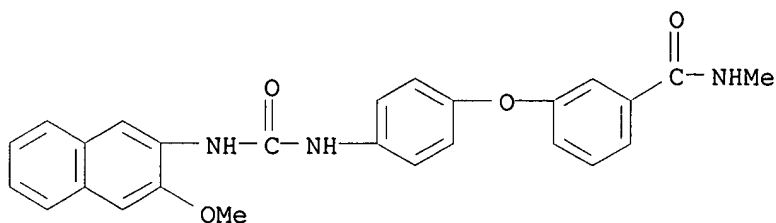
CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-ethyl- (9CI) (CA INDEX NAME)



RN 284462-34-6 CAPLUS

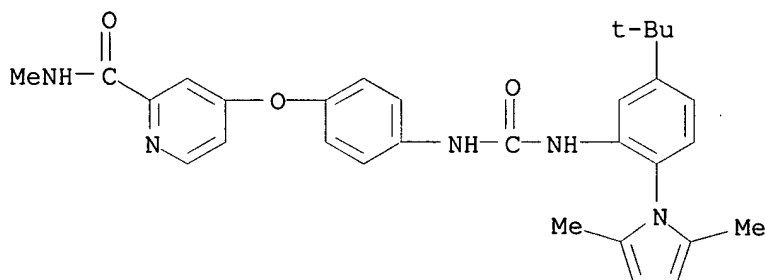
CN Benzamide, 3-[4-[[[3-methoxy-2-naphthalenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)





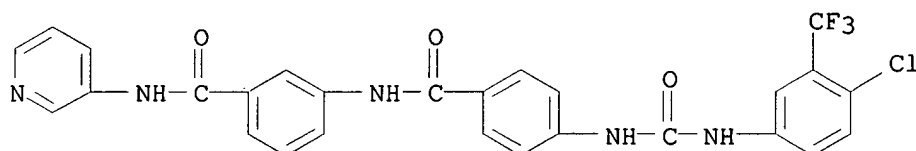
RN 284462-35-7 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[5-(1,1-dimethylethyl)-2-(2,5-dimethyl-1H-pyrrol-1-yl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



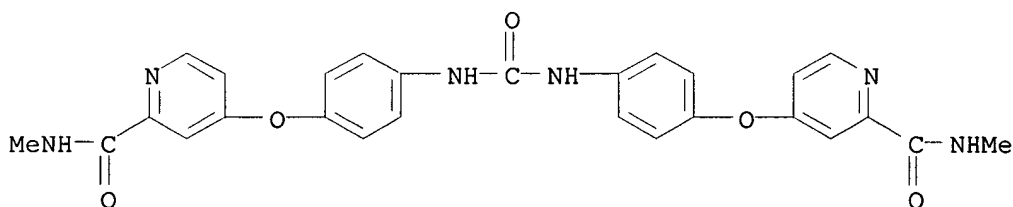
RN 284462-70-0 CAPLUS

CN Benzamide, 3-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]benzoyl]amino]-N-3-pyridinyl- (9CI) (CA INDEX NAME)



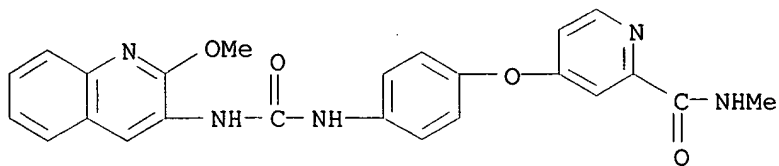
RN 284670-98-0 CAPLUS

CN 2-Pyridinecarboxamide, 4,4'-[carbonylbis(imino-4,1-phenyleneoxy)]bis[N-methyl- (9CI) (CA INDEX NAME)



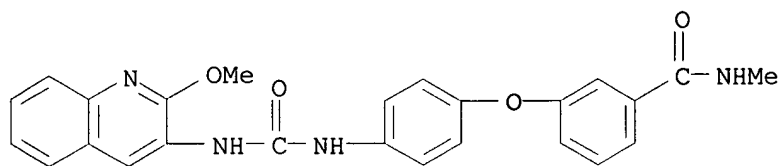
RN 432050-22-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-3-quinolinyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



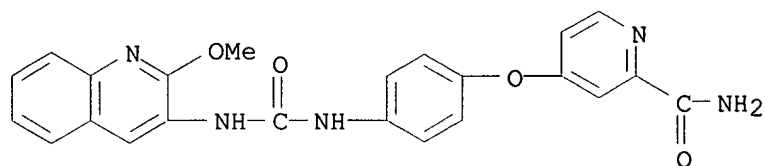
RN 432050-23-2 CAPLUS

CN Benzamide, 3-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



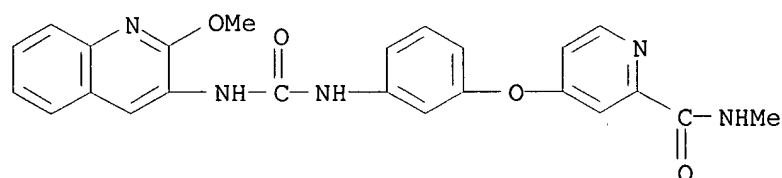
RN 432050-24-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



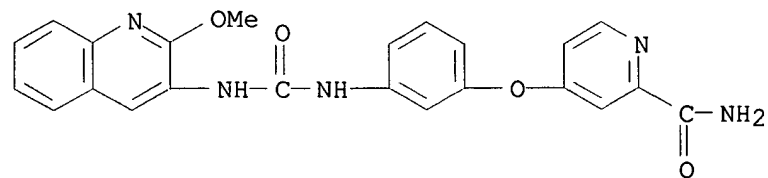
RN 432050-25-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 432050-26-5 CAPLUS

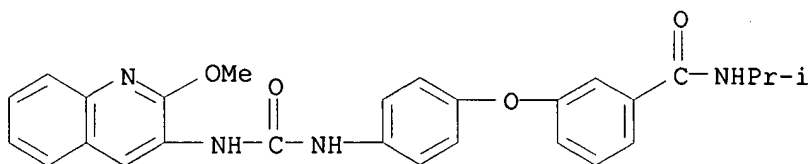
CN 2-Pyridinecarboxamide, 4-[3-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



RN 432050-27-6 CAPLUS

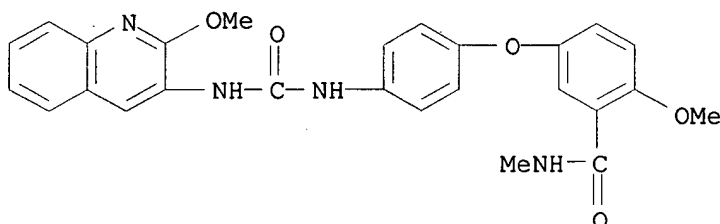
CN Benzamide, 3-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-

(1-methylethyl)- (9CI) (CA INDEX NAME)



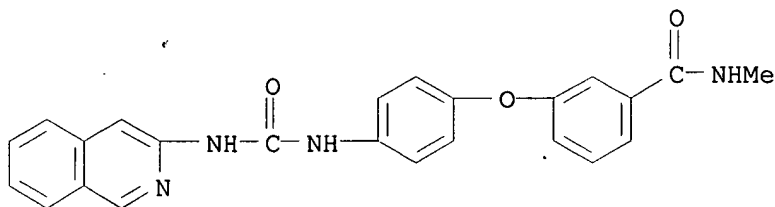
RN 432050-28-7 CAPLUS

CN Benzamide, 2-methoxy-5-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



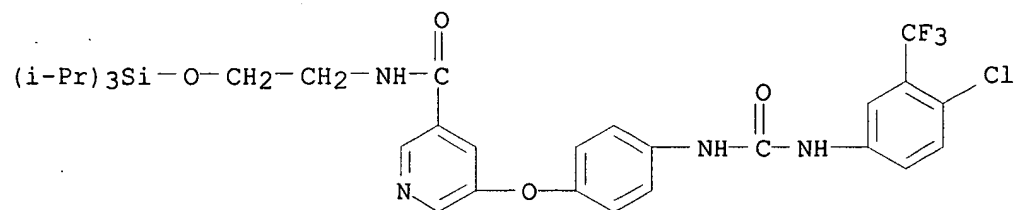
RN 432050-52-7 CAPLUS

CN Benzamide, 3-[4-[[[(3-isoquinolinylamino)carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



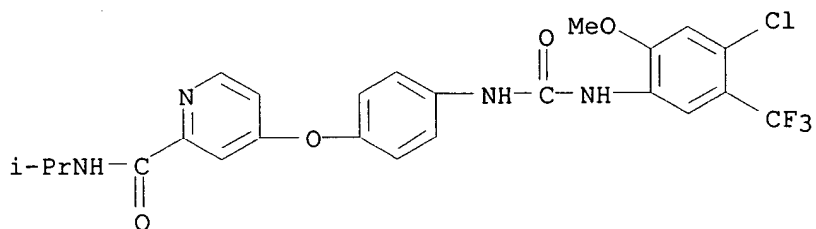
RN 447457-08-1 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-[[tris(1-methylethyl)silyl]oxy]ethyl]- (9CI) (CA INDEX NAME)



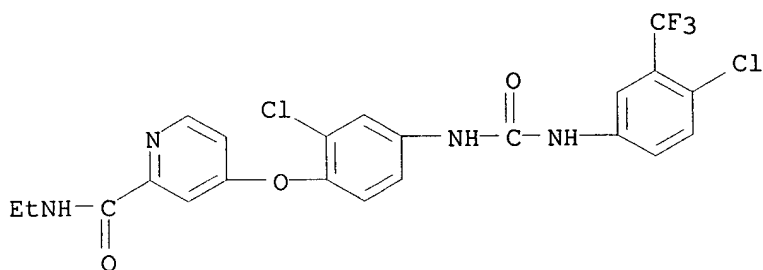
RN 447457-09-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 474642-44-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[2-chloro-4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-ethyl- (9CI) (CA INDEX NAME)

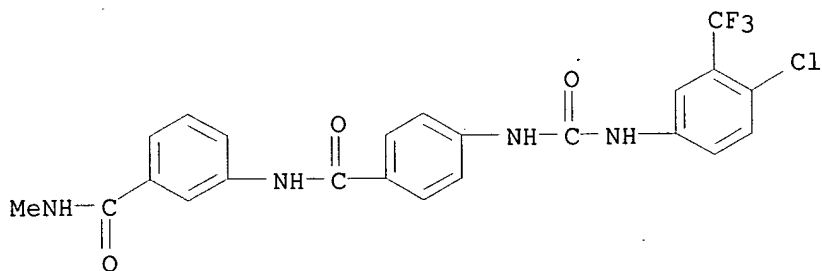


IT 284461-99-0P 284462-71-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(intermediate; prepn. of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf kinase)

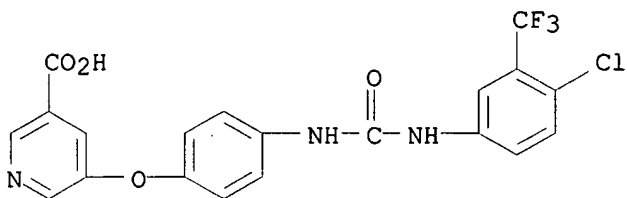
RN 284461-99-0 CAPLUS

CN Benzamide, 3-[[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]benzoyl]amino]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-71-1 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



IT 139691-76-2, Raf kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(prepn. of quinolyl, isoquinolyl or pyridyl-ureas as **inhibitors**  
of raf kinase)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

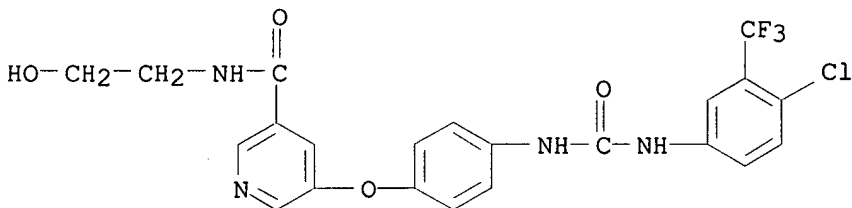
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 474642-55-2

RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf  
kinase)

RN 474642-55-2 CAPLUS

CN 3-Pyridinecarboxamide, 5-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



L122 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:785445 CAPLUS

DOCUMENT NUMBER: 138:296904

TITLE: BAY 43-9006: Preclinical data

AUTHOR(S): Wilhelm, Scott; Chien, Du-Shieng

CORPORATE SOURCE: ~~Bayer Research Center~~, Institute for Preclinical Drug  
Development, Pharmaceutical Division, Bayer  
Corporation, West Haven, CT, 06516, USA

SOURCE: Current Pharmaceutical Design (2002), 8(25), 2255-2257  
CODEN: CPDEFP; ISSN: 1381-6128

PUBLISHER: Bentham Science Publishers

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

ED Entered STN: 15 Oct 2002

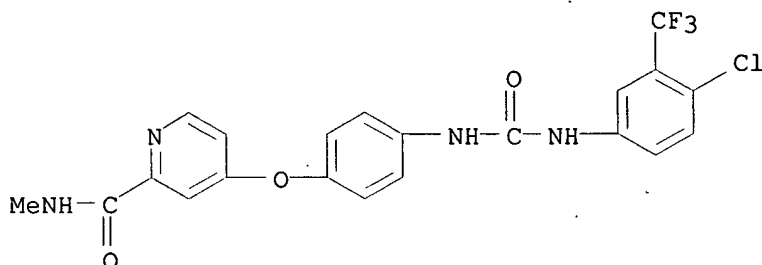
AB A review. The drug design and discovery efforts described in the previous section led to the development of a novel, small mol. Raf-1 kinase inhibitor, BAY 43-9006, which belongs to a class that can be broadly described as bis-aryl ureas. BAY 43-9006 was identified during a large medicinal chem. optimization program, and this compd. was selected for further pharmacol. characterization based on its potent inhibition of Raf-1 (IC50 12 nM) and its favorable kinase selectivity profile [2, 3]. In vitro and in vivo expts. were designed to demonstrate effective blockade of the Raf/MEK/ERK signaling pathway in tumor cells and for antitumor efficacy in human xenograft models.

IT 284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(antitumor BAY 43-9006)

RN 284461-73-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
arbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



IT 139691-76-2, Raf-1 kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; antitumor BAY 43-9006)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L122 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:785444 CAPLUS

DOCUMENT NUMBER: 137:362317

TITLE: BAY 43-9006: Early clinical data in patients with  
advanced solid malignancies

AUTHOR(S): Hotte, Sebastien J.; Hirte, Hal W.

CORPORATE SOURCE: Department of Medicine, Hamilton Regional Cancer  
Centre, McMaster University and Division of Medical  
Oncology, Hamilton, ON, Can.

SOURCE: Current Pharmaceutical Design (2002), 8(25), 2249-2253  
CODEN: CPDEFP; ISSN: 1381-6128

PUBLISHER: Bentham Science Publishers

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

ED Entered STN: 15 Oct 2002

AB A review. Various signaling pathways can confer the malignant phenotype to a cell. Ras signaling proteins have been found to play an important role in controlling cellular growth. Raf-1 is a protein kinase that exerts its effects downstream of Ras in the mitogen-activated protein kinase pathway and is thus likely to be crucial in the development of the malignant phenotype. BAY 43-9006 is an orally administered selective inhibitor of Raf-1 and the first compd. of its class to enter clin. trials. This article describes the early clin. data of BAY 43-9006 in patients with advanced, refractory solid tumors. To date, over 60 patients have been treated as part of four Phase I clin. trials. Dose levels have ranged from 50mg once weekly to 200mg twice-daily in continuous administration. The drug has been generally well tolerated with no dose limiting toxicity yet encountered. The more common toxicities have involved the gastrointestinal tract (diarrhea, nausea, abdominal cramping) and the skin (pruritus, rash, cheilitis). Pharmacokinetic evaluations have found BAY 43-9006 to have considerable interpatient variability. However, there seems to be an increase in Cmax and AUC values with increasing dose. There is no clear effect of food on

bioavailability. Splitting the dose to twice-daily administration has shown increases in Cmax and AUC values but is also accompanied by considerable interpatient variability.

IT 475207-59-1, BAY 43-9006 mono-p-tosylate

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(BAY 43-9006 for patients with advanced solid neoplasm)

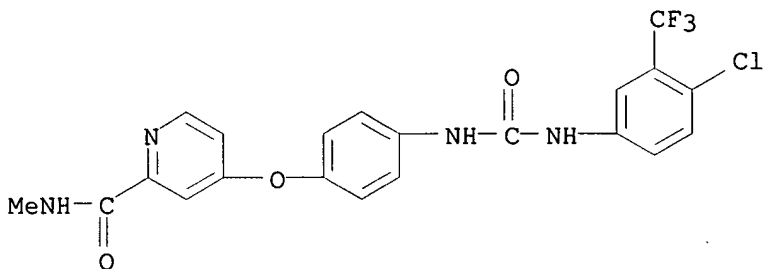
RN 475207-59-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

CRN 284461-73-0

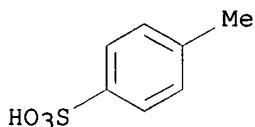
CMF C21 H16 Cl F3 N4 O3



CM 2

CRN 104-15-4

CMF C7 H8 O3 S



IT 139691-76-2, Raf-1 kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor; BAY 43-9006 for patients with advanced solid neoplasm)

RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L122 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:208292 CAPLUS

DOCUMENT NUMBER: 139:269975

TITLE: Oncolytic Raf kinase inhibitor

AUTHOR(S): Sorbera, L. A.; Castaner, J.; Bozzo, J.; Leeson, P. A.

CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain

SOURCE: Drugs of the Future (2002), 27(12), 1141-1147

Searched by Barb O'Bryen, STIC 571-272-2518

PUBLISHER: CODEN: DRFUD4; ISSN: 0377-8282  
DOCUMENT TYPE: Prous Science  
LANGUAGE: Journal; General Review  
English

ED Entered STN: 18 Mar 2003

AB A review with refs. The Ras/Raf/MEK pathway is a signaling module that controls cell growth and survival. Activation of this pathway results in a cascade of events from the cell surface to the nucleus ultimately affecting cellular proliferation, apoptosis, differentiation and transformation. Raf is a serine/threonine kinase that is a downstream effector enzyme of Ras. When activated, Raf goes on to activate MEK1 and MEK2 kinases which in turn phosphorylate and activate ERK1 and ERK2 which translocate to the nucleus where they stimulate pathways required for translation initiation and transcription activation leading to proliferation. Raf kinase has been validated as a potential and attractive target for hyperproliferative disorders such as cancer. Research has recently focused on efforts to discover potent Raf kinase inhibitors and several low-mol.-wt. Raf kinase inhibitors have been described. Bis-aryl ureas were identified within this program using medicinal chem.-directed syntheses or combinatorial libraries. After high-throughput screening of more than 200,000 compds. against recombinant Raf-1 kinase, the orally active Bay-43-9006 was identified as having potent inhibitory activity and was chosen for further development as a treatment for cancer. Bay-43-9006 has exhibited potent in vitro activity against several tumor cell lines and has displayed efficacy in human tumor xenograft models. Moreover, results from phase I development in patients with a variety of cancer types indicates promising clin. efficacy for the compd.

IT 139691-76-2, Raf kinase 284461-73-0, Bay-43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(oncolytic Raf kinase inhibitor)

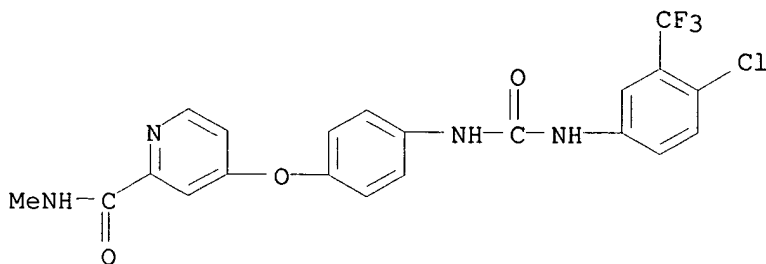
RN 139691-76-2 CAPLUS

CN Kinase (phosphorylating), gene raf-1 protein (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 284461-73-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
arbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L122 ANSWER 20 OF 28

MEDLINE on STN

DUPLICATE 1

ACCESSION NUMBER: 2002002443 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11751484

TITLE: PNU-145156E, a novel angiogenesis inhibitor, in patients



AUTHOR: with solid tumors: a phase I and pharmacokinetic study.  
Groen H J; de Vries E G; Wynendaele W; van der Graaf W T;  
Fokkema E; Lechuga M J; Poggesi I; Dirix L Y; van Oosterom  
A T

CORPORATE SOURCE: Department of Pulmonary Diseases, University Hospital  
Groningen, Hanzeplein 1, 9713 GZ Groningen, the  
Netherlands.. h.j.m.groen@int.azg.nl

SOURCE: Clinical cancer research : an official journal of the  
American Association for Cancer Research, (2001 Dec) 7 (12)  
3928-33.  
Journal code: 9502500. ISSN: 1078-0432.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)  
(CLINICAL TRIAL, PHASE I)  
Journal; Article; (JOURNAL ARTICLE)  
(MULTICENTER STUDY)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200203

ENTRY DATE: Entered STN: 20020102  
Last Updated on STN: 20020403  
Entered Medline: 20020327

## ABSTRACT:

Our aim was to establish, in patients with solid tumors, the dose-limiting toxicity, maximum tolerated dose (MTD), and pharmacology of PNU-145156E, a new sulfonated distamycin A derivative that blocked circulating angiogenesis-promoting growth factors in animal studies and exhibited an antitumor effect in murine solid tumors. In a Phase I study, PNU-145156E was administered i.v. every 6 weeks. Included were patients with solid tumors; an Eastern Cooperative Oncology Group performance score  $\leq 1$ ; and normal bone marrow, renal, and liver functions and blood clotting tests. Excluded were patients with brain metastases or on steroid medication. Toxicity was scored with the National Cancer Institute Common Toxicity Criteria. Plasma and urine PNU-145156E was measured for pharmacokinetic analysis. The effect of PNU-145156E on serum basic fibroblast growth factor (bFGF) was measured by sandwich ELISA. Twenty-nine patients (median age, 54 years; range, 33-71 years; 19 males and 10 females; median performance score = 1) were treated at dose levels of 100-1050 mg/m<sup>2</sup>. We observed, during 47 treatment cycles, erratic but short-lasting decreases of antithrombin III levels ( $<75\%$ ) at all dose levels. Other clotting tests remained normal except during thromboembolic events. Dose-limiting toxicity was thrombophlebitis, pulmonary embolism, and grade 3 dyspnea. PNU-145156E disappeared from the circulation, decreasing triexponentially with a long terminal half-life of 1 month. No significant change in bFGF and no objective tumor responses were observed. Disease stabilization was achieved in four patients. In conclusion, the MTD of PNU-145156E was 1050 mg/m<sup>2</sup>. Serum bFGF level was not affected by PNU-145156E up to the MTD.

CONTROLLED TERM: Check Tags: Female; Human; Male; Support, Non-U.S. Gov't  
Adult  
Aged  
\*Angiogenesis Inhibitors: AE, adverse effects  
Angiogenesis Inhibitors: BL, blood  
\*Angiogenesis Inhibitors: PK, pharmacokinetics  
Area Under Curve  
Blood Coagulation: DE, drug effects  
\*Distamycins: AE, adverse effects  
Distamycins: BL, blood  
\*Distamycins: PK, pharmacokinetics  
Dose-Response Relationship, Drug  
Infusions, Intravenous  
Metabolic Clearance Rate  
Middle Aged  
Neoplasms: BL, blood

**\*Neoplasms: DT, drug therapy**

Patient Selection

CAS REGISTRY NO.:

154788-16-6 (FCE 26644)

CHEMICAL NAME:

0 (Angiogenesis Inhibitors); 0 (Distamycins)

L122 ANSWER 21 OF 28

MEDLINE on STN

DUPLICATE 2

ACCESSION NUMBER:

2000302179

MEDLINE

DOCUMENT NUMBER:

PubMed ID: 10845556

TITLE:

Antiangiogenic, antitumoural and antimetastatic effects of two distamycin A derivatives with anti-HIV-1 Tat activity in a Kaposi's sarcoma-like murine model.

AUTHOR:

Rossati L; Campioni D; Sola F; Leone L; Ferrante L; TrabANELLI C; Ciomei M; Montesi M; Rocchetti R; Talevi S; Bompadre S; Caputo A; Barbanti-Brodano G; Corallini A

CORPORATE SOURCE:

Institute of Biomedical Sciences, University of Ancona, Italy.. possati@popcsi.unian.it

SOURCE:

Clinical & experimental metastasis, (1999) 17 (7) 575-82.  
Journal code: 8409970. ISSN: 0262-0898.

PUB. COUNTRY:

Netherlands

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals; AIDS

ENTRY MONTH:

200006

ENTRY DATE:

Entered STN: 20000706

Last Updated on STN: 20000706

Entered Medline: 20000627

**ABSTRACT:**

The antiangiogenic, antitumoural and antimetastatic effects of two novel sulphonc derivatives of distamycin A, PNU145156E and PNU153429, were studied in a Kaposi's sarcoma-like tumour model obtained by injecting nude mice with cells releasing extracellular HIV-Tat protein, derived from a tumour which developed in a BK virus/tat transgenic mouse. Both PNU145156E and PNU153429 were administered intraperitoneally every fourth day for three weeks at doses of 100 or 50 mg/kg of body weight respectively, starting one day after injecting the tumour cells. Both drugs delayed tumour growth in nude mice, preventing neovascularization induced by the Tat protein. PNU153429 also significantly reduced the number and size of spontaneous tumour metastases. Both effects on tumour growth and metastases were augmented by treating simultaneously nude mice with 7.5 mg/kg of body weight of minocycline given per os daily for four weeks starting four days after injecting the tumour cells. Neither acute nor chronic toxic side-effects were observed during the life span of treated nude mice. Due to their antiangiogenic and anti-Tat effects, these drugs are promising for the treatment of Kaposi's sarcoma in AIDS patients.

CONTROLLED TERM:

Check Tags: Female; Male; Support, Non-U.S. Gov't

Angiogenesis Inhibitors: PD, pharmacology

\*Angiogenesis Inhibitors: TU, therapeutic use

Angiogenesis Inhibitors: TO, toxicity

Animals

Antineoplastic Agents: PD, pharmacology

\*Antineoplastic Agents: TU, therapeutic use

Antineoplastic Agents: TO, toxicity

Antineoplastic Combined Chemotherapy Protocols: TU, therapeutic use

Distamycins: AD, administration &amp; dosage

Distamycins: PD, pharmacology

\*Distamycins: TU, therapeutic use

Distamycins: TO, toxicity

Drug Screening Assays, Antitumor

\*Gene Products, tat: AI, antagonists &amp; inhibitors

Genes, tat

\*HIV-1: GE, genetics

Mice

Mice, Nude

Mice, Transgenic  
Minocycline: AD, administration & dosage  
\*Neoplasm Metastasis: DT, drug therapy  
\*Neoplasm Proteins: AI, antagonists & inhibitors  
Neoplasm Transplantation  
\*Neovascularization, Pathologic: DT, drug therapy  
\*Sarcoma, Kaposi: DT, drug therapy  
Sarcoma, Kaposi: ET, etiology  
Sarcoma, Kaposi: PA, pathology  
Transfection  
CAS REGISTRY NO.: 10118-90-8 (Minocycline); 154788-16-6 (FCE 26644)  
CHEMICAL NAME: 0 (Angiogenesis Inhibitors); 0 (Antineoplastic Agents); 0  
(Antineoplastic Combined Chemotherapy Protocols); 0  
(Distamycins); 0 (Gene Products, tat); 0 (Neoplasm  
Proteins); 0 (PNU 153429)

L122 ANSWER 22 OF 28 MEDLINE on STN DUPLICATE 3  
ACCESSION NUMBER: 1999380181 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10449994  
TITLE: Effects of suramin on anastomotic colon tumors in  
a rat model.  
AUTHOR: Lauwers P; Hubens G; Hendriks J; Vermeulen P; Schuerwegh A;  
Stevens W J; De Clerck L S; Dirix L; Van Marck E; Hubens A;  
Eyskens E  
CORPORATE SOURCE: Laboratory for Experimental Surgery and Department of  
Immunology, 'Medisch Instituut Sint Augustinus', Antwerp,  
Belgium.  
SOURCE: European surgical research. Europäische chirurgische  
Forschung. Recherches chirurgicales europeennes, (1999) 31:  
(4) 347-56.  
Journal code: 0174752. ISSN: 0014-312X.  
PUB. COUNTRY: Switzerland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199910  
ENTRY DATE: Entered STN: 19991101  
Last Updated on STN: 19991101  
Entered Medline: 19991021

## ABSTRACT:

BACKGROUND: The development of antiangiogenic drugs offers new promise in the treatment of malignancy. Suramin has been reported to inhibit tumor growth by blocking angiogenesis and has been used in clinical trials. The aim of the present study was to examine the effects of suramin on colonic anastomotic tumors in the rat. METHODS: (a) Colonic anastomotic tumor was induced in 120 WAG/RIJ rats. Half of the animals were given 100 mg/kg of suramin intraperitoneally at the time of tumor induction. Rats were sacrificed after 2, 4 and 8 weeks; tumor take and tumor weight were evaluated. (b) The number of red blood cell clusters per x 400 field was counted in each tumor. (c) A lymphocyte transformation test was performed in four groups of animals, 2 weeks before and 2 weeks after tumor implantation and/or suramin administration. RESULTS: (a) A significant enhancement of tumor growth was observed in the suramin-treated animals. (b) This was accompanied by a significant increase in functional blood vessels. (c) Suramin-treated rats had markedly decreased lymphocyte stimulation, pointing to a possible immunosuppressive effect. CONCLUSIONS: The growth of an anastomotic \*\*\*colon\*\*\* tumor is rather enhanced by a single intraperitoneal administration of 100 mg/kg suramin in the rat, possibly by an unexpected immunosuppressive effect.

CONTROLLED TERM: Check Tags: Comparative Study; Male  
Adenocarcinoma: BS, blood supply  
\*Adenocarcinoma: DT, drug therapy  
Adenocarcinoma: IM, immunology

Adenocarcinoma: PA, pathology  
Anastomosis, Surgical: AE, adverse effects  
Animals  
\*Antineoplastic Agents: PD, pharmacology  
Cell Survival: DE, drug effects  
Colon: PA, pathology  
\*Colon: SU, surgery  
Colonic Neoplasms: BS, blood supply  
\*Colonic Neoplasms: DT, drug therapy  
Colonic Neoplasms: IM, immunology  
Colonic Neoplasms: PA, pathology  
Lymphocyte Activation: IM, immunology  
Neoplasm Transplantation  
Neoplasms, Experimental: BS, blood supply  
\*Neoplasms, Experimental: DT, drug therapy  
Neoplasms, Experimental: IM, immunology  
Neoplasms, Experimental: PA, pathology  
Neovascularization, Pathologic: IM, immunology  
Neovascularization, Pathologic: PA, pathology  
Random Allocation  
Rats  
Rats, Inbred Strains  
\*Suramin: PD, pharmacology  
Tumor Cells, Cultured  
CAS REGISTRY NO.: 145-63-1 (Suramin)  
CHEMICAL NAME: 0 (Antineoplastic Agents)

L122 ANSWER 23 OF 28 MEDLINE on STN DUPLICATE 4  
ACCESSION NUMBER: 97285161 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9140434  
TITLE: Suramin in non-small cell lung cancer and  
advanced breast cancer. Two parallel phase II studies.  
AUTHOR: Mirza M R; Jakobsen E; Pfeiffer P; Lindebjerg-Clasen B;  
Bergh J; Rose C  
CORPORATE SOURCE: Department of Oncology, Odense University Hospital,  
Denmark.  
SOURCE: Acta oncologica (Stockholm, Sweden), (1997) 36 (2) 171-4.  
Journal code: 8709065. ISSN: 0284-186X.  
PUB. COUNTRY: Norway  
DOCUMENT TYPE: (CLINICAL TRIAL)  
(CLINICAL TRIAL, PHASE II)  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199705  
ENTRY DATE: Entered STN: 19970609  
Last Updated on STN: 19970609  
Entered Medline: 19970528

## ABSTRACT:

Suramin inhibits the growth of non-small cell lung cancer (NSCLC) and breast cancer in vitro by blocking the action of most known growth factors. The clinical efficacy of suramin was evaluated in patients with unresectable or relapsed NSCLC (n = 16) and advanced breast cancer (ABC) resistant to conventional therapies (n = 12). A plasma level > or = 200 micrograms/ml was maintained by three times weekly administrations using adaptive control with feedback. Treatment was continued until documented progression of disease or unacceptable toxicity. No clinical responses were observed in any patient. Median overall survival was 4.5 months in NSCLC and 9 months in ABC patients. Mean treatment duration was 6.6 weeks in NSCLC patients and 15.9 weeks in ABC patients. Treatment was discontinued due to disease progression in 14 patients, unacceptable adverse effects in 11 patients, while three patients refused to continue therapy. We cannot recommend this drug for further clinical trials in NSCLC and ABC.

CONTROLLED TERM: Check Tags: Female; Human; Male  
Adult  
Aged  
Antineoplastic Agents: AE, adverse effects  
Antineoplastic Agents: BL, blood  
\*Antineoplastic Agents: TU, therapeutic use  
Breast Neoplasms: BL, blood  
\*Breast Neoplasms: DT, drug therapy  
Carcinoma, Non-Small-Cell Lung: BL, blood  
\*Carcinoma, Non-Small-Cell Lung: DT, drug therapy  
Lung Neoplasms: BL, blood  
\*Lung Neoplasms: DT, drug therapy  
Middle Aged  
Suramin: AE, adverse effects  
Suramin: BL, blood  
\*Suramin: TU, therapeutic use  
CAS REGISTRY NO.: 145-63-1 (Suramin)  
CHEMICAL NAME: 0 (Antineoplastic Agents)

L122 ANSWER 24 OF 28 MEDLINE on STN DUPLICATE 5  
ACCESSION NUMBER: 97230207 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9075785  
TITLE: Suramin inhibits the growth of non-small-cell lung cancer cells that express the epidermal growth factor receptor.  
AUTHOR: Fujiuchi S; Ohsaki Y; Kikuchi K  
CORPORATE SOURCE: First Department of Medicine, Asahikawa Medical College, Japan.  
SOURCE: Oncology, (1997 Mar-Apr) 54 (2) 134-40.  
Journal code: 0135054. ISSN: 0030-2414.  
PUB. COUNTRY: Switzerland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199704  
ENTRY DATE: Entered STN: 19970422  
Last Updated on STN: 20000303  
Entered Medline: 19970408

## ABSTRACT:

The epidermal growth factor (EGF) is a potent growth factor that is believed to enhance the proliferation of cancer cells by a paracrine or autocrine mechanism. EGF transduces various signals and finally stimulates cell proliferation upon binding to cell surface receptors. Prevention of the association of this peptide with its receptors might lead to the development of new modalities for treatment of lung cancer. Several investigators have reported that suramin has antiproliferative activity against cancer cells that express EGF receptors (EGF-R), and that it acts by blocking the binding of the ligand to its receptor. In this study, we analyzed the antitumor effect of suramin using two lines of lung cancer cells (A549 and PC-13), which express EGF-R, and a variety of assays. Receptor-binding assays confirmed that A549 and PC-13 cells have cell surface receptors for EGF. Suramin inhibited the binding of EGF to these receptors. EGF and fetal bovine serum (FBS) stimulated the proliferation of cells, but suramin inhibited these effects in a dose-dependent fashion. Suramin at 200 microg/ml reduced the growth of A549 and PC-13 cells by 25 and 15%, respectively, in medium that contained 1% FBS. Paradoxically, the concentrations of suramin that inhibited cell proliferation were lower than those that were effective in inhibiting the binding of EGF to its receptor. Although expression of c-fos and c-myc mRNA increased when cells were stimulated by EGF or FBS, suramin at 200 microg/ml did not markedly alter such expression. Suramin partially blocked the EGF-induced progression of the cell cycle from the G0/G1 to the S phase. These results suggest that suramin partially blocks EGF signal transduction. Suramin probably inhibits cell proliferation by inhibiting intranuclear enzymes, as well as by partial

blockage of EGF signal transduction.

CONTROLLED TERM: Check Tags: Human  
\*Anticarcinogenic Agents: PD, pharmacology  
Blotting, Northern  
\*Carcinoma, Non-Small-Cell Lung: DT, drug therapy  
\*Carcinoma, Non-Small-Cell Lung: ME, metabolism  
Cell Division: DE, drug effects  
\*Gene Expression Regulation, Neoplastic: DE, drug effects  
Genes, fos  
Genes, myc  
\*Lung Neoplasms: DT, drug therapy  
\*Lung Neoplasms: ME, metabolism  
RNA, Messenger: ME, metabolism  
RNA, Neoplasm: ME, metabolism  
\*Receptor, Epidermal Growth Factor: BI, biosynthesis  
Receptor, Epidermal Growth Factor: ME, metabolism  
\*Suramin: PD, pharmacology  
Tumor Cells, Cultured  
CAS REGISTRY NO.: 145-63-1 (Suramin)  
CHEMICAL NAME: 0 (Anticarcinogenic Agents); 0 (RNA, Messenger); 0 (RNA, Neoplasm); EC 2.7.1.112 (Receptor, Epidermal Growth Factor)

L122 ANSWER 25 OF 28 MEDLINE on STN DUPLICATE 6  
ACCESSION NUMBER: 96336811 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8738403  
TITLE: Intravesical suramin: a novel agent for the treatment of superficial transitional-cell carcinoma of the bladder.  
AUTHOR: Walther M M; Figg W D; Linehan W M  
CORPORATE SOURCE: Urologic Oncology Section, National Cancer Institute, Bethesda, MD 20892, USA.  
SOURCE: World journal of urology, (1996) 14 Suppl 1 S8-11. Ref: 31  
Journal code: 8307716. ISSN: 0724-4983.  
PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199612  
ENTRY DATE: Entered STN: 19970128  
Last Updated on STN: 19970128  
Entered Medline: 19961202

ABSTRACT:

Patients with recurrent or high-grade superficial transitional-cell carcinoma of the **bladder** that has recurred after intravesical chemotherapy are at increased risk for tumor invasion and metastases. Intravesical chemotherapy is a minimally invasive technique that allows high doses of therapeutic agents to be delivered directly to the malignancy, doses that would not be tolerated systemically. In vitro studies demonstrate suramin's significant efficacy against transitional-cell carcinoma cell lines at relatively low doses. Humans treated with similar doses delivered in a systemic fashion have experienced no \*\*\*bladder\*\*\* toxicity. Suramin has been shown to block the binding of epidermal growth factor (EGF) to its receptors, which are found in large amounts in **bladder** cancers. Because a significant association has been found between the number of EGF receptors on a **bladder**-cancer cell and its sensitivity to suramin, transitional-cell carcinoma could potentially be very responsive to such therapy. On the basis of these findings, a phase I escalating-suramin-dose study is currently being conducted.

CONTROLLED TERM: Check Tags: Human  
Administration, Intravesical  
Animals  
Antineoplastic Agents: AD, administration & dosage

\*Antineoplastic Agents: TU, therapeutic use  
\*Bladder Neoplasms: DT, drug therapy  
\*Carcinoma, Transitional Cell: DT, drug therapy  
Suramin: AD, administration & dosage  
\*Suramin: TU, therapeutic use

Treatment Outcome

CAS REGISTRY NO.: 145-63-1 (Suramin)  
CHEMICAL NAME: 0 (Antineoplastic Agents)

L122 ANSWER 26 OF 28 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 91003939 MEDLINE

DOCUMENT NUMBER: PubMed ID: 2208069

TITLE: The concentration of glucose in the culture medium determines the effect of suramin on the growth and differentiation of the human colonic adenocarcinoma cell clone HT29-D4.

AUTHOR: Rabenandrasana C; Baghdiguian S; Roccabianca M; Brunet M; Marvaldi J; Fantini J

CORPORATE SOURCE: CNRS URA 202, Universite de Provence, Marseille, France.

SOURCE: Cancer letters, (1990 Sep) 53 (2-3) 109-15.  
Journal code: 7600053. ISSN: 0304-3835.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199011

ENTRY DATE: Entered STN: 19910117  
Last Updated on STN: 19970203  
Entered Medline: 19901115

ABSTRACT:

Suramin, a drug currently used for advanced malignancy, induces the differentiation of the human colonic adenocarcinoma cell clone HT29-D4 and this process is correlated with a decreased glycolytic activity. We investigated the effects of suramin on HT29-D4 cells in the presence of various glucose concentrations. The main result of this study is that suramin has only an effect on HT29-D4 cell growth and differentiation when the concentration of glucose is above 10 mM. Therefore the efficiency of suramin as an anticancer drug may be greater on poorly differentiated tumoral cells with a high proliferative capacity.

CONTROLLED TERM: Check Tags: Human; In Vitro; Support, Non-U.S. Gov't.

\*Adenocarcinoma: DT, drug therapy

Adenocarcinoma: ME, metabolism

\*Colonic Neoplasms: DT, drug therapy

Colonic Neoplasms: ME, metabolism

Culture Media

Glucose: ME, metabolism

\*Glucose: PD, pharmacology

Microscopy, Electron

\*Suramin: TU, therapeutic use

\*Tumor Cells, Cultured: DE, drug effects

Tumor Cells, Cultured: ME, metabolism

CAS REGISTRY NO.: 145-63-1 (Suramin); 50-99-7 (Glucose)

CHEMICAL NAME: 0 (Culture Media)

L122 ANSWER 27 OF 28 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 89170311 MEDLINE

DOCUMENT NUMBER: PubMed ID: 2924693

TITLE: [Treatment of metastatic adrenal carcinoma with suramin].  
Behandlung des metastasierten Nebennierenkarzinoms mit Suramin.

AUTHOR: Allolio B; Jaursch-Hancke C; Reincke M; Arlt W; Metzler U; Winkelmann W

CORPORATE SOURCE: Medizinische Universitätsklinik II und Poliklinik, Koln.

SOURCE: Deutsche medizinische Wochenschrift, (1989 Mar 10) 114 (10)  
381-4.  
Journal code: 0006723. ISSN: 0012-0472.  
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of  
DOCUMENT TYPE: (CASE REPORTS)  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: German  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198904  
ENTRY DATE: Entered STN: 19900306  
Last Updated on STN: 19900306  
Entered Medline: 19890427

## ABSTRACT:

A right adrenocortical carcinoma (weighing 978 g) was removed from a 45-year-old man in April 1986, the tumour bed then being irradiated with 40 Gy. Subsequently discovered multiple lung metastases were treated with cisplatin, etoposide and bleomycin, without improvement. Treatment with mitotane (Lysodren) was also without effect and had to be discontinued because of severe side effects. Treatment with suramin (Germanin) was begun in August 1987. After a loading dose of 10.7 g for six weeks the lung metastases regressed almost completely. But lung metastases were again demonstrated in January 1988 during a low-dose maintenance regimen of suramin. Increased dosage arrested further growth, but achieved no regression of the metastases. The patient died unexpectedly in April 1988 of acute circulatory failure. Suramin administration had been discontinued six weeks earlier because of bronchopneumonia and general deterioration. Thrombocytopenia, coagulation disorders and moderate proteinuria were the side effects of suramin treatment.

CONTROLLED TERM: Check Tags: Comparative Study; Human; Male  
Adrenal Cortex Neoplasms: BL, blood  
\*Adrenal Cortex Neoplasms: DT, drug therapy  
Antineoplastic Combined Chemotherapy Protocols: AE, adverse effects  
Antineoplastic Combined Chemotherapy Protocols: TU, therapeutic use  
Carcinoma: BL, blood  
\*Carcinoma: DT, drug therapy  
Combined Modality Therapy  
Dose-Response Relationship, Drug  
Drug Evaluation  
English Abstract  
Lung Neoplasms: BL, blood  
Lung Neoplasms: DT, drug therapy  
\*Lung Neoplasms: SC, secondary  
Middle Aged  
Radiotherapy Dosage  
Remission Induction  
Suramin: AD, administration & dosage  
Suramin: AE, adverse effects  
\*Suramin: TU, therapeutic use  
Time Factors

CAS REGISTRY NO.: 145-63-1 (Suramin)  
CHEMICAL NAME: 0 (Antineoplastic Combined Chemotherapy Protocols)

L122 ANSWER 28 OF 28 MEDLINE on STN  
ACCESSION NUMBER: 2002729156 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12478189  
TITLE: A phase I study of intravesical suramin for the treatment of superficial transitional cell carcinoma of the bladder.  
AUTHOR: Uchio Edward M; Linehan W Marston; Figg William D; Walther McClellan M  
CORPORATE SOURCE: Urologic Oncology Therapeutic Branch, Center for Cancer



SOURCE: Research, National Cancer Institute/NIH, Bethesda, MD, USA.  
Journal of urology, (2003 Jan) 169 (1) 357-60.  
Journal code: 0376374. ISSN: 0022-5347.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)  
(CLINICAL TRIAL, PHASE I)  
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200301

ENTRY DATE: Entered STN: 20021221  
Last Updated on STN: 20030110  
Entered Medline: 20030109

## ABSTRACT:

**PURPOSE:** Suramin is a polysulfonated naphthylurea that inhibits proliferation and DNA synthesis of transitional cell carcinoma cell lines. Its large molecular size and negative charge inhibit **bladder** absorption, making suramin an excellent candidate for intravesical chemotherapy. Intravesical suramin was evaluated in a phase I study to define dose limiting toxicity and systemic absorption, determine a starting dose and regimen for phase II studies and provide a preliminary assessment of in vivo antitumor activity. **MATERIALS AND METHODS:** Intravesical suramin treatment was administered in 9 patients with histologically identified transitional cell carcinoma (Tcis, Ta or T1) in whom at least 1 course of standard intravesical chemotherapy (bacillus Calmette-Guerin, thiotepa or mitomycin C) had failed. Suramin was administered once weekly for 6 weeks. Patients were treated in groups of 3 using a 60 cc volume and inpatient dose escalation schedule. Suramin doses of 0.3 to 614.4 mg./ml. were administered intravesically. The last group was treated with the same weekly dose for 6 weeks. **RESULTS:** The 9 patients underwent 54 treatments with suramin. Plasma suramin concentration after treatment was 1.9 to 38.0 microg./ml. and was not related to treatment dose. The dose escalation phase was limited by the solubility of suramin in solution. Complications included self-limited **bladder** spasms (less than 24 hours) in 4 of 54 treatments (7%) and new or worsening vesicoureteral reflux in 3 ureters (17%). Another patient who was treated after the Foley balloon was inflated in the urethra experienced **bladder** spasms, skin flushing and fever (39C). Mean **bladder** capacity before and after treatment was 600 and 540 ml., respectively. At followup 7 patients had stage Ta tumors and 2 had carcinoma in situ. **CONCLUSIONS:** An intravesical suramin dose of 153 mg./ml was defined as a safe treatment parameter with acceptable plasma concentrations and minimal side effects. Phase II studies are needed to assess the antitumor activity of suramin in patients with transitional cell carcinoma of the **bladder**.

**CONTROLLED TERM:** Check Tags: Female; Human; Male; Support, U.S. Gov't, P.H.S.

Administration, Intravesical  
Aged

\*Antineoplastic Agents: AD, administration & dosage  
Antineoplastic Agents: AE, adverse effects

\***Bladder Neoplasms:** DT, drug therapy

**Bladder Neoplasms:** PA, pathology

\***Carcinoma, Transitional Cell:** DT, drug therapy

Carcinoma, Transitional Cell: PA, pathology

Middle Aged

\***Suramin:** AD, administration & dosage

**Suramin:** AE, adverse effects

CAS REGISTRY NO.: 145-63-1 (Suramin)  
CHEMICAL NAME: 0 (Antineoplastic Agents)

=> fil reg

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DICTIONARY FILE UPDATES: 8 MAR 2004 HIGHEST RN 660388-34-1

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<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> s 145-63-1 or 154788-16-6

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1 154788-16-6  
(154788-16-6/RN)  
L123 2 145-63-1 OR 154788-16-6

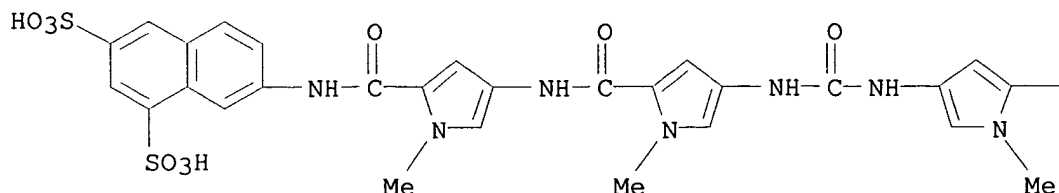
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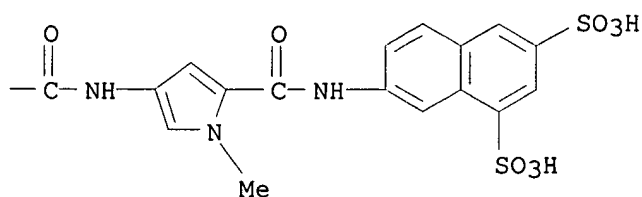
L123 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN  
RN **154788-16-6** REGISTRY  
CN 1,3-Naphthalenedisulfonic acid, 7,7'-[carbonylbis[imino(1-methyl-1H-pyrrole-4,2-diyl)carbonylimino(1-methyl-1H-pyrrole-4,2-diyl)carbonylimino]]bis-, tetrasodium salt (9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN FCE 26644  
CN PNU 145156E  
CN PNU 151484  
MF C45 H40 N10 O17 S4 . 4 Na  
SR CA  
LC STN Files: ADISINSIGHT, BIOSIS, CA, CANCERLIT, CAPLUS, IMSDRUGNEWS, IMSRESEARCH, MEDLINE, PHAR, PROMT, TOXCENTER, USPATFULL  
CRN (159537-58-3)

PAGE 1-A



● 4 Na

PAGE 1-B



24 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

24 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L123 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN

RN 145-63-1 REGISTRY

CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis- (9CI)  
(CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[ureylenebis[m-phenylenecarbonylimino(4-methyl-m-phenylene)carbonylimino]]di- (8CI)

OTHER NAMES:

CN 8,8'-[Ureylenebis[m-phenylenecarbonylimino(4-methyl-m-phenylene)carbonylimino]]di-1,3,5-naphthalenetrisulfonic acid

CN Farma

CN Farma 939

CN Fourneau

CN Naganol

CN Suramin

CN Suramine

MF C51 H40 N6 O23 S6

CI COM

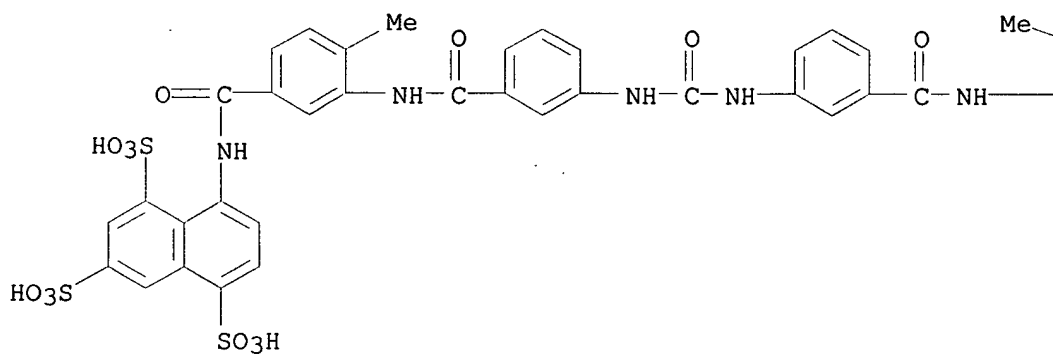
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(\*File contains numerically searchable property data)

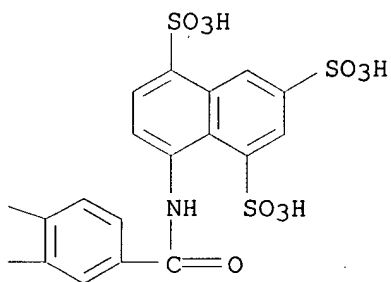
Other Sources: EINECS\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

PAGE 1-A



PAGE 1-B



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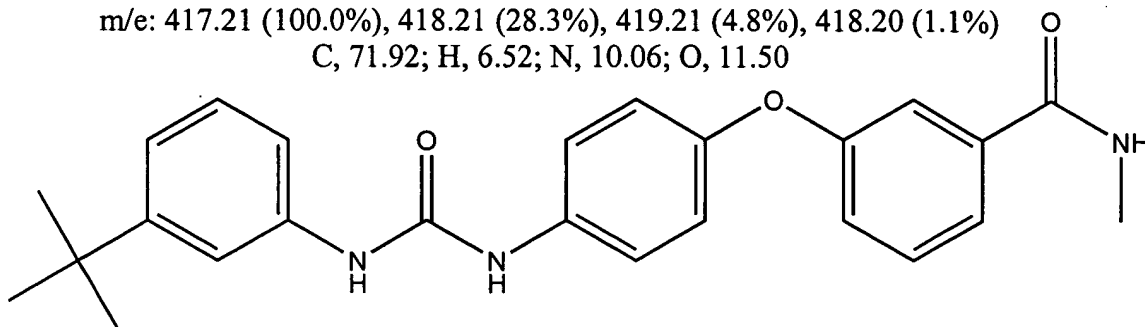
37 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1332 REFERENCES IN FILE CAPLUS (1907 TO DATE)

3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

$C_{25}H_{27}N_3O_3$   
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Mol. Wt.: 417.50

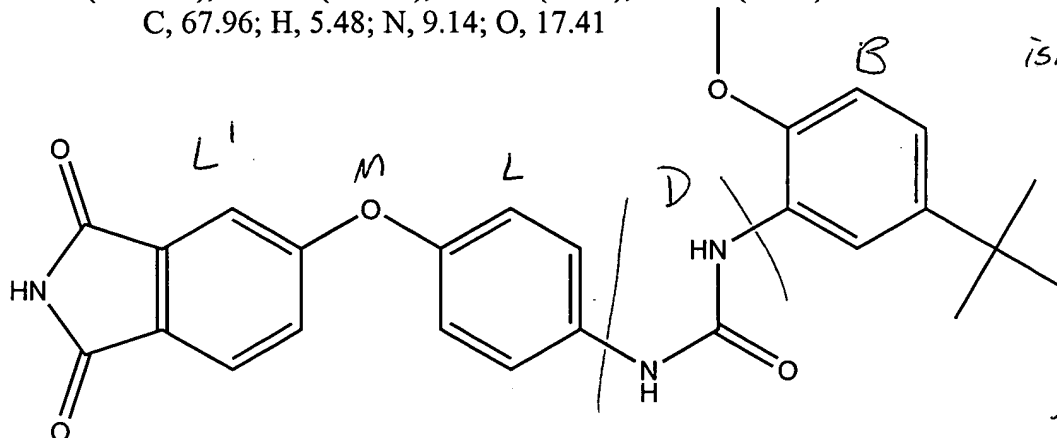
m/e: 417.21 (100.0%), 418.21 (28.3%), 419.21 (4.8%), 418.20 (1.1%)  
C, 71.92; H, 6.52; N, 10.06; O, 11.50



n-(3-tert-butylphenyl)-n'-(4-(3-(n-methylcarbamoyl)phenoxy)phenyl) urea

$C_{26}H_{25}N_3O_5$   
Exact Mass: 459.18  
Mol. Wt.: 459.49

m/e: 459.18 (100.0%), 460.18 (30.2%), 461.19 (4.2%), 461.18 (1.3%)  
C, 67.96; H, 5.48; N, 9.14; O, 17.41



n-(5-tert-butyl-2-methoxyphenyl)-n'-(4-(1,3-dioxoisindolin-5-yloxy)phenyl) urea

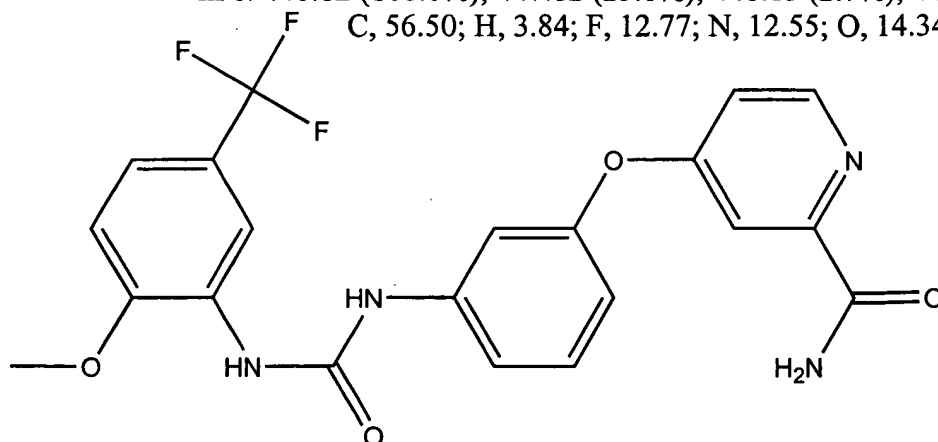
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isn't covered by  
claim 1*

*L' lacks  
specified  
substituents*

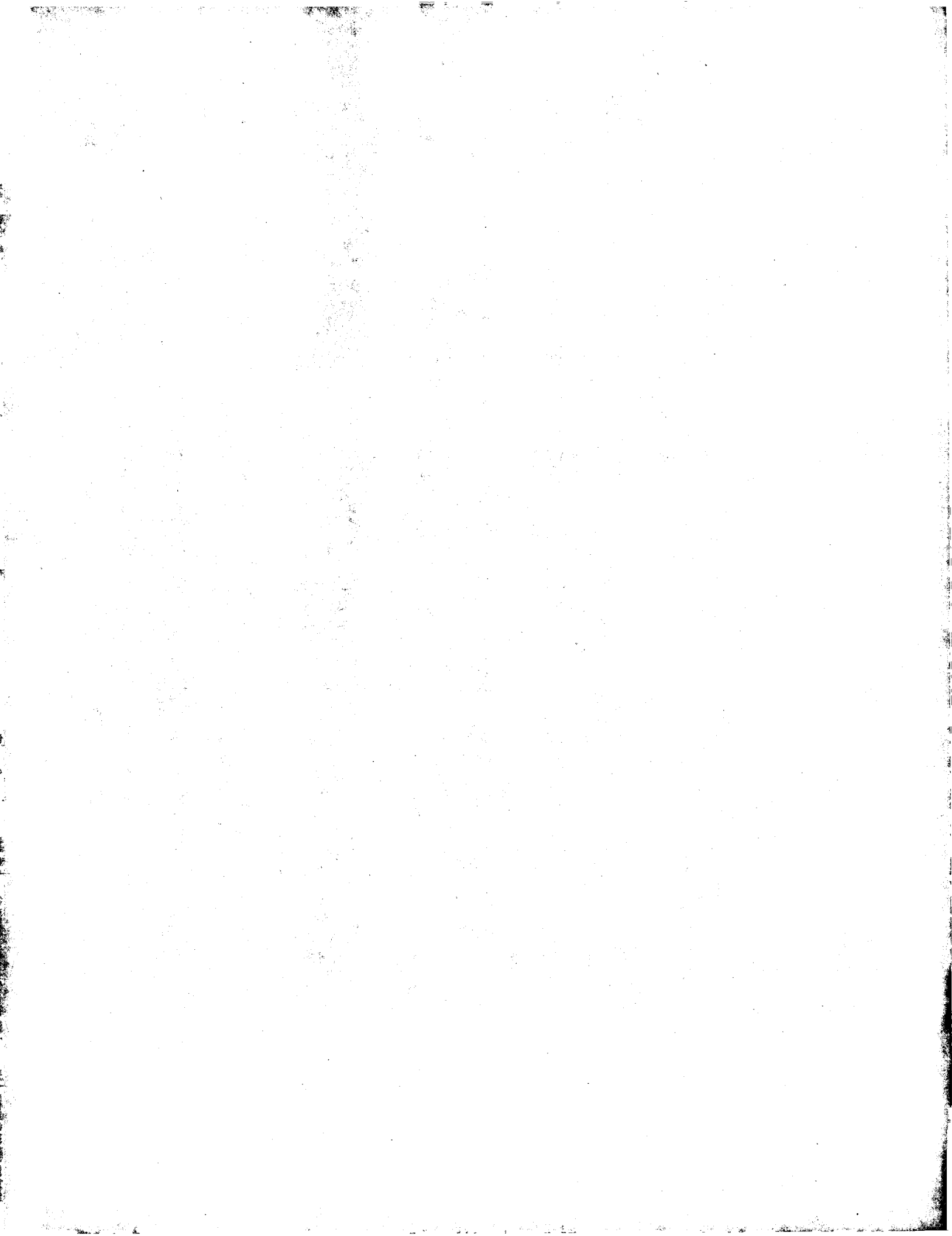
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claim 1, I guess  
it doesn't matter)*

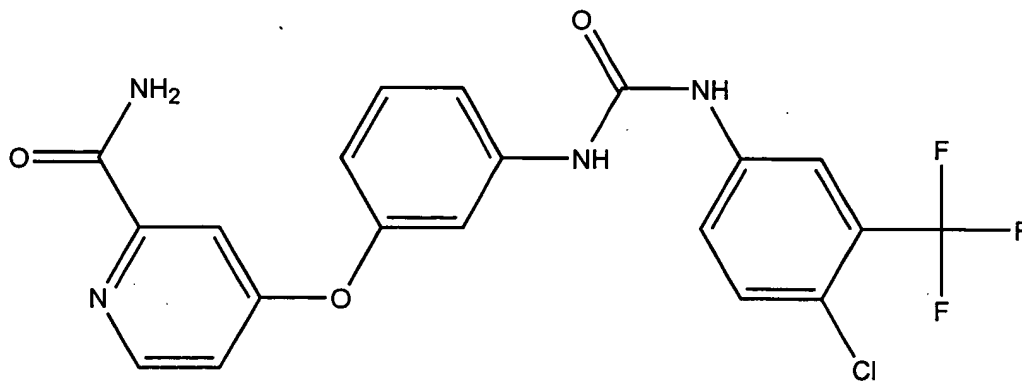
$C_{21}H_{17}F_3N_4O_4$   
Exact Mass: 446.12  
Mol. Wt.: 446.38

m/e: 446.12 (100.0%), 447.12 (25.0%), 448.13 (2.7%), 448.12 (1.2%)  
C, 56.50; H, 3.84; F, 12.77; N, 12.55; O, 14.34



n-(2-methoxy-5-(trifluoromethyl)phenyl)-n'-(3-(2-carbamoyl-4-pyridyloxy)phenyl)urea





n-(4-chloro-3-(trifluoromethyl)phenyl)-n'-(3-(2-carbamoyl-4-pyridoxy)phenyl)urea

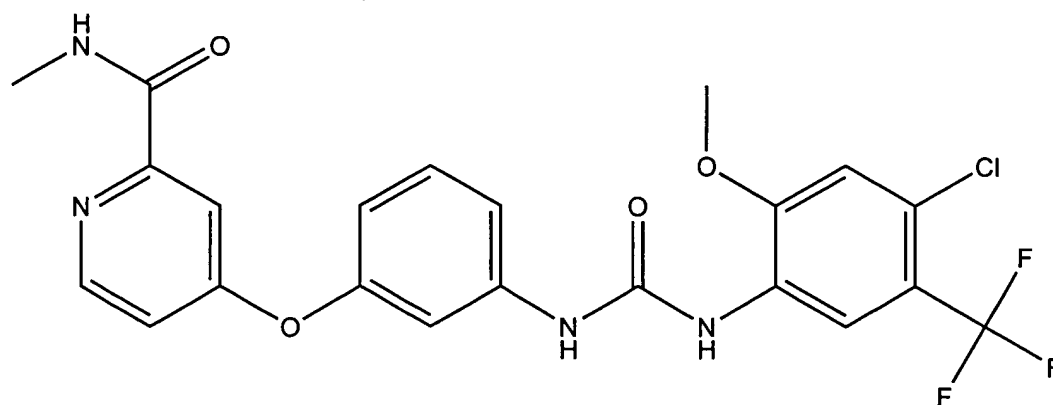
$C_{20}H_{14}ClF_3N_4O_3$

Exact Mass: 450.07

Mol. Wt.: 450.80

m/e: 450.07 (100.0%), 452.07 (32.9%), 451.07 (23.9%), 453.07 (7.3%), 452.08 (2.4%),  
454.07 (1.1%)

C, 53.29; H, 3.13; Cl, 7.86; F, 12.64; N, 12.43; O, 10.65



n-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-n'-(3-(2-(n-methylcarbamoyl)-4-pyridyloxy)phenyl)urea

$C_{22}H_{18}ClF_3N_4O_4$

Exact Mass: 494.10

Mol. Wt.: 494.85

m/e: 494.10 (100.0%), 496.09 (32.0%), 495.10 (24.9%), 497.10 (8.2%), 496.10 (4.1%), 495.09  
(1.5%), 498.10 (1.2%)

C, 53.40; H, 3.67; Cl, 7.16; F, 11.52; N, 11.32; O, 12.93

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=> fil reg; d stat que l118; fil capl uspatf toxcenter; s l118  
FILE 'REGISTRY' ENTERED AT 17:01:48 ON 09 MAR 2004  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

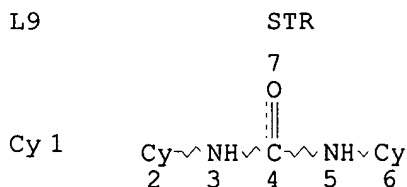
STRUCTURE FILE UPDATES: 8 MAR 2004 HIGHEST RN 660388-34-1  
DICTIONARY FILE UPDATES: 8 MAR 2004 HIGHEST RN 660388-34-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more  
information enter HELP PROP at an arrow prompt in the file or refer  
to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

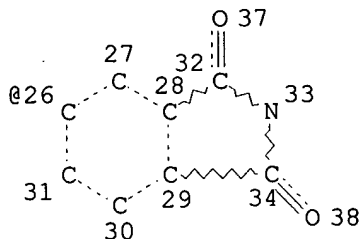
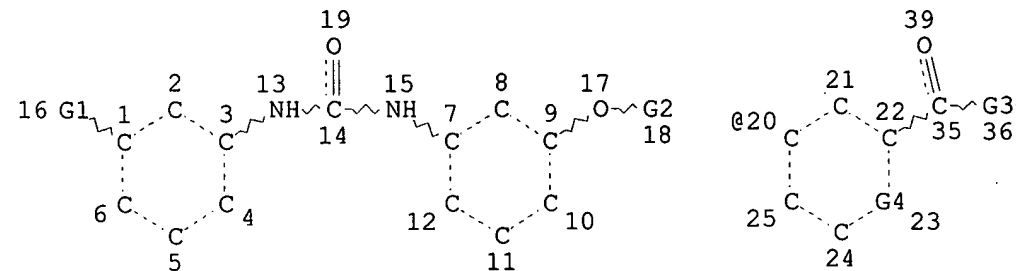


*same full file search as  
before*

NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 7

STEREO ATTRIBUTES: NONE  
L11 7207318 SEA FILE=REGISTRY ABB=ON NR>2 AND N>1 AND O/ELS  
L13 40386 SEA FILE=REGISTRY SUB=L11 SSS FUL L9  
L116 STR



NH~Me  
@40 41

*subset search done on  
this structure  
(highlighted compounds)*

VAR G1=T-BU/CF3

VAR G2=20/26

VAR G3=NH2/40

VAR G4=N/C

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 41

STEREO ATTRIBUTES: NONE

L118 9 SEA FILE=REGISTRY SUB=L13 SSS FUL L116

100.0% PROCESSED 51 ITERATIONS

SEARCH TIME: 00.00.01

9 ANSWERS

FILE 'CAPLUS' ENTERED AT 17:01:49 ON 09 MAR 2004

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FILE 'USPATFULL' ENTERED AT 17:01:49 ON 09 MAR 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'TOXCENTER' ENTERED AT 17:01:49 ON 09 MAR 2004

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L124 26 L118

=> dup rem l124

PROCESSING COMPLETED FOR L124

L125 16 DUP REM L124 (10 DUPLICATES REMOVED)

ANSWERS '1-7' FROM FILE CAPLUS

## ANSWERS '8-16' FROM FILE USPATFULL

=> d ibib ed abs hitstr 1-16; fil hom

L125 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1  
ACCESSION NUMBER: 2003:874965 CAPLUS  
DOCUMENT NUMBER: 139:364958  
TITLE: Preparation of omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors  
INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.  
PATENT ASSIGNEE(S): Bayer Corporation, USA  
SOURCE: U.S. Pat. Appl. Publ., 60 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003207872	A1	20031106	US 2002-42226	20020111
PRIORITY APPLN. INFO.:			US 2002-42226	20020111

OTHER SOURCE(S): MARPAT 139:364958

ED Entered STN: 07 Nov 2003

AB Urea derivs. of formula A-NHCONH-B or pharmaceutically acceptable salts thereof [A = a substituted moiety of up to 40 carbon atoms of the formula -L-(M-L1)q; where L = a 5 or 6 membered cyclic structure bound directly to D; L1 = a substituted cyclic moiety having at least 5 members; M = a bridging group having at least one atom; q = an integer of 1-3; each cyclic structure of L and L1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur; B = a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D contg. 0-4 members of the group consisting of nitrogen, oxygen and sulfur] are prepd. These compds. are useful for raf mediated diseases, in particular a cancerous cell growth mediated by raf kinase. All compds. exemplified, e.g. N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea, displayed IC50 of between 1 mM and 10 .mu.M.

IT 284461-42-3P 284461-43-4P 284461-49-0P

284461-75-2P 284461-76-3P 284461-81-0P

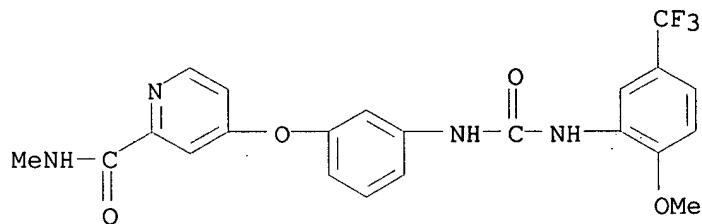
284462-22-2P 284462-23-3P 284462-31-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of .omega.-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)

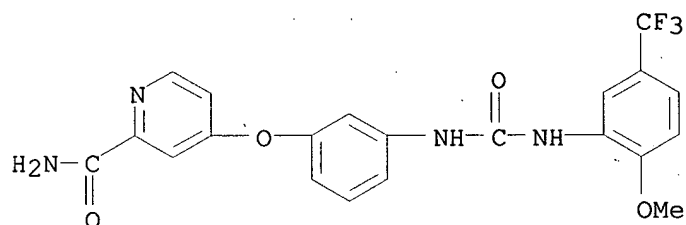
RN 284461-42-3 CAPLUS

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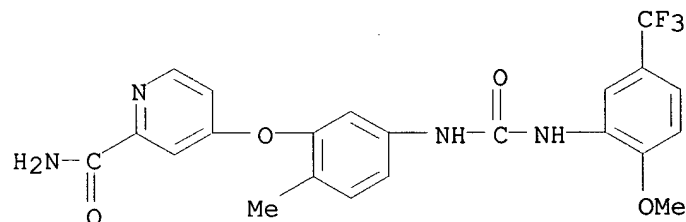
RN 284461-43-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



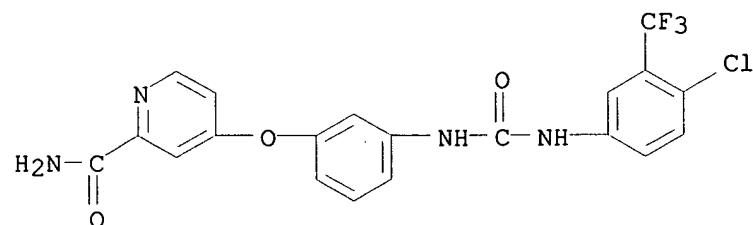
RN 284461-49-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]- (9CI) (CA INDEX NAME)



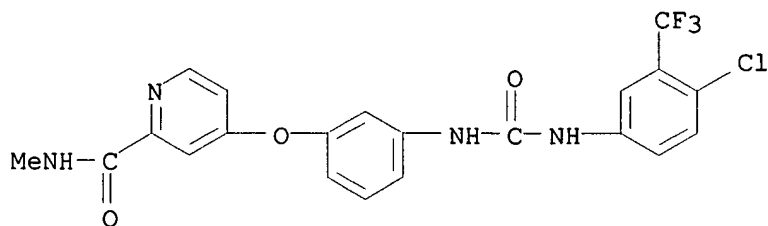
RN 284461-75-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



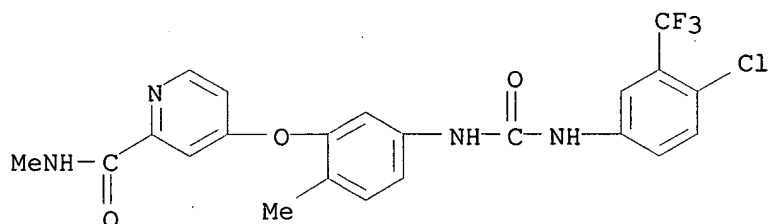
RN 284461-76-3 CAPLUS

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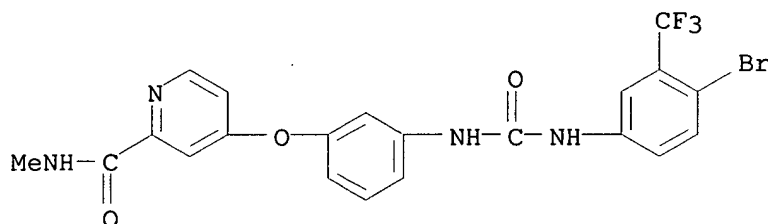
RN 284461-81-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



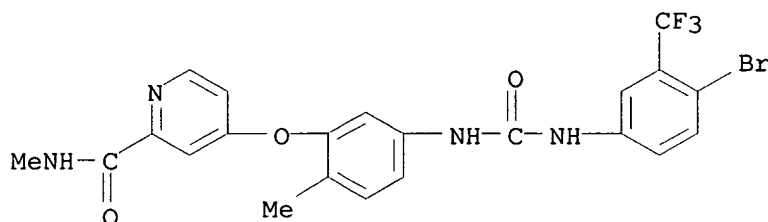
RN 284462-22-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



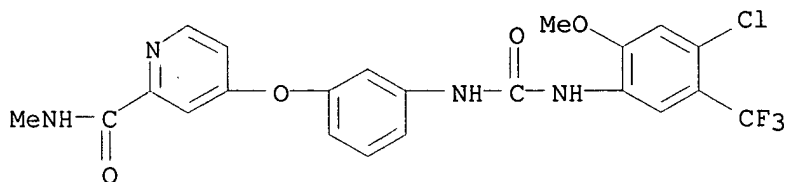
RN 284462-23-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



L125 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2  
 ACCESSION NUMBER: 2003:757329 CAPLUS  
 DOCUMENT NUMBER: 139:276918  
 TITLE: Preparation of omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors  
 INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.  
 PATENT ASSIGNEE(S): Bayer Corporation, USA  
 SOURCE: U.S. Pat. Appl. Publ., 61 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003/181442	A1	20030925	US 2001-993647	20011127
PRIORITY APPLN. INFO.:			US 2001-993647	20011127
OTHER SOURCE(S): MARPAT 139:276918				

ED Entered STN: 26 Sep 2003

AB Aryl ureas of formula A-NHCONH-B [A = a substituted moiety of up to 40 carbon atoms of the formula: -L-(M-L1)<sub>q</sub> (where L = a 5 or 6 membered cyclic structure bound directly to D, L1 comprises a substituted cyclic moiety having at least 5 members; M = a bridging group having at least one atom; q = an integer of from 1-3; each cyclic structure of L and L1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur); B = a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D contg. 0-4 members of the group consisting of nitrogen, oxygen and sulfur] are prepd. These urea derivs. are useful for treating raf mediated diseases, in particular cancerous cell growth mediated by raf kinase. Thus, N-[4-bromo-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea. Thus, a soln. of 4-bromo-3-(trifluoromethyl)phenyl isocyanate (8.0 g, 30.1 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (80 mL) was added dropwise to a soln. of 4-[2-(N-methylcarbamoyl)-4-pyridyloxy]aniline (7.0 g, 28.8 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (40 mL) at 0.degree., stirred at room temp. for 16 h, and filtered to give, after washing the yellow solids, washing with CH<sub>2</sub>Cl<sub>2</sub> (2 .times. 50 mL), and drying under reduced pressure (approx. 1 mmHg) at 40.degree. to give N-[4-bromo-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea. All compds. exemplified showed IC<sub>50</sub> between 1 nM to 10 .mu.M against raf kinase.

IT **284461-42-3P 284461-43-4P**, N-(2-Methoxy-5-trifluoromethylphenyl)-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea  
**284461-49-0P**, N-(2-Methoxy-5-trifluoromethylphenyl)-N'-[3-[(2-carbamoyl-4-pyridyl)oxy]-4-methylphenyl]urea **284461-75-2P**,  
 N-(4-Chloro-3-trifluoromethylphenyl)-N'-[3-[(2-carbamoyl-4-pyridyl)oxy]phenyl]urea **284461-76-3P**, N-(4-Chloro-3-

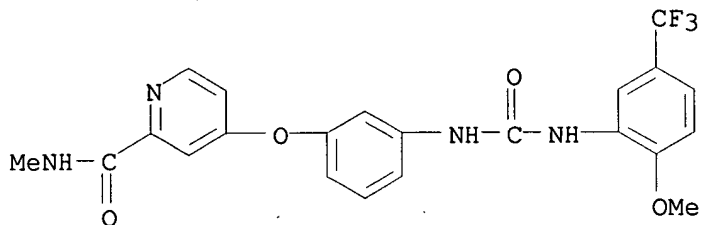
trifluoromethylphenyl)-N'-[3-[(2-methylcarbamoyl-4-pyridyl)oxy]phenyl]urea  
284461-81-OP 284462-22-2P 284462-23-3P  
284462-31-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(prepn. of omega-carboxyaryl substituted di-Ph ureas as raf kinase  
inhibitors and anticancer agents)

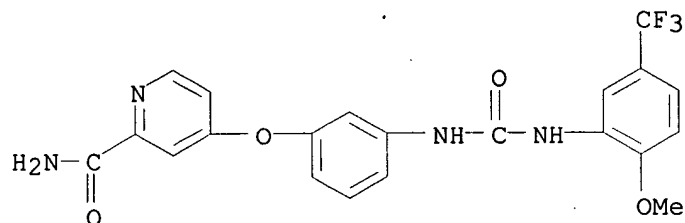
RN 284461-42-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]  
carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



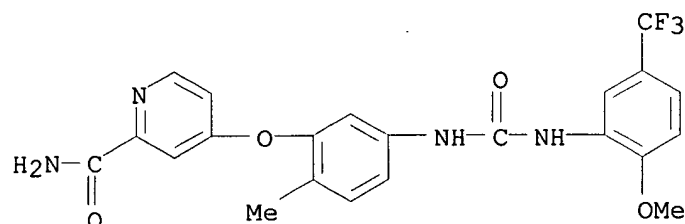
RN 284461-43-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]  
carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



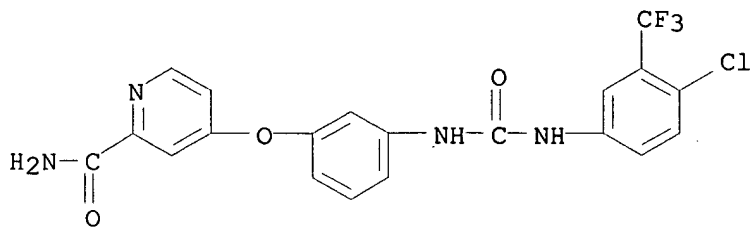
RN 284461-49-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]  
carbonyl]amino]-2-methylphenoxy]- (9CI) (CA INDEX NAME)



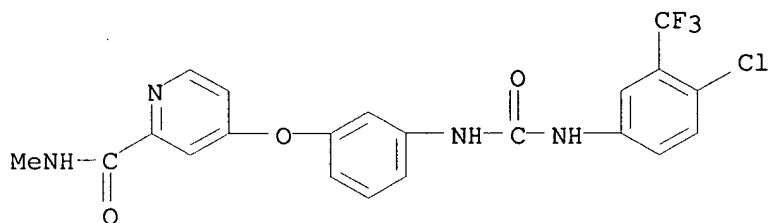
RN 284461-75-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
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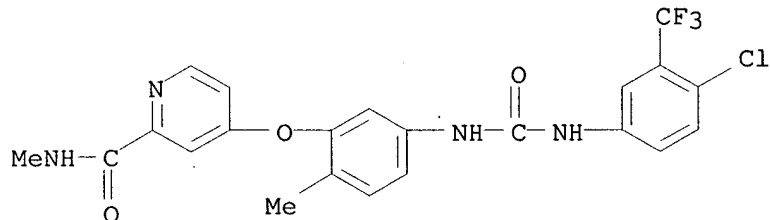
RN 284461-76-3 CAPLUS

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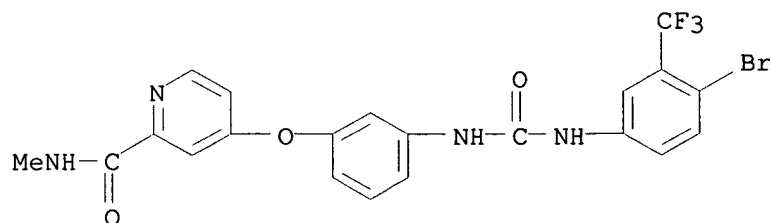
RN 284461-81-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-22-2 CAPLUS

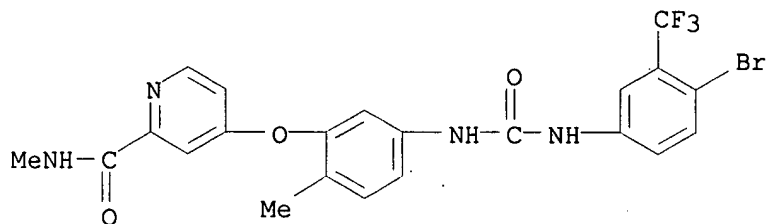
CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



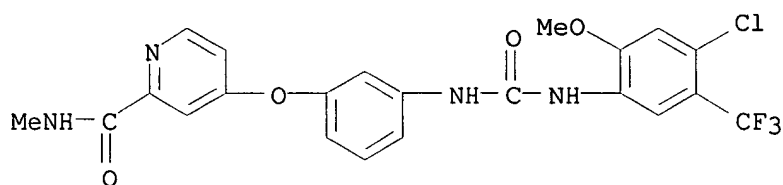
RN 284462-23-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)





RN 284462-31-3 CAPLUS  
 CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



L125 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3  
 ACCESSION NUMBER: 2003:590832 CAPLUS  
 DOCUMENT NUMBER: 139:149528  
 TITLE: Preparation of diphenylureas as RAF kinase inhibitors  
 INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.  
 PATENT ASSIGNEE(S): Bayer Corporation, USA  
 SOURCE: U.S. Pat. Appl. Publ., 62 pp., Cont. of U. S. Ser. No. 42,203.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

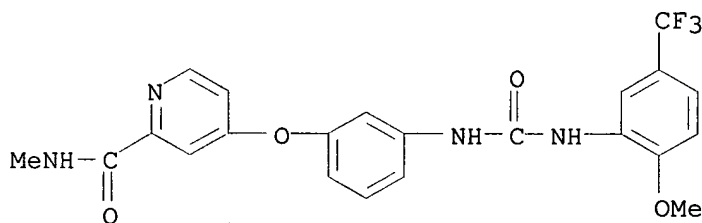
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003144278	A1	20030731	US 2002-283248	20021030
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			US 2002-42203	A1 20020111

OTHER SOURCE(S): MARPAT 139:149528

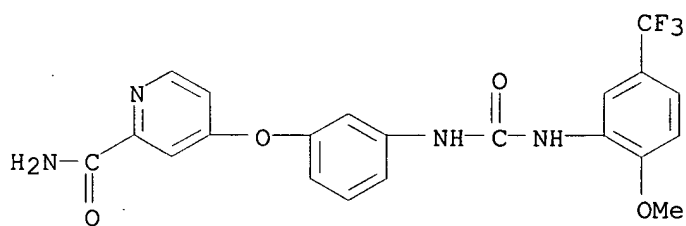
ED Entered STN: 01 Aug 2003

AB ADB [I; D = NHCONH; A = L(ML1)q; L = 5-6 membered cyclic structure bound directly to D; L1 = substituted cyclic moiety having .gtoreq.5 members, M = bridging group having .gtoreq.1 atom; q = 1-3; L, L1 contain 0-4 N, O, S; B = (substituted) up to tricyclic aryl, heteroaryl of .ltoreq.30 C atoms with .gtoreq.1 6-membered cyclic structure bound directly to D contg. 0-4 N, O, S], were prepd. Thus, 4-chloro-3-(trifluoromethyl)phenyl isocyanate in CH2Cl2 was added dropwise to a suspension of 4-[2-(N-methylcarbamoyl)-4-pyridyloxy]aniline (prepn. given) in CH2Cl2 at 0.degree.; the resulting mixt. was stirred at room temp. for 22 h. to afford N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea. I inhibited RAF kinase in the range 1 nM-1 .mu.M. I pharmaceutical compns. are claimed.

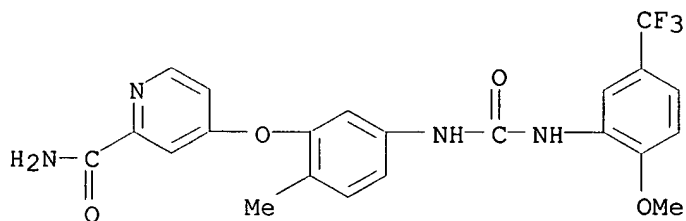
IT **284461-42-3P**, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea **284461-43-4P**, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl] urea **284461-49-0P** **284461-75-2P**, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl] urea **284461-76-3P**, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea **284461-81-0P** **284462-22-2P**, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea **284462-23-3P** **284462-31-3P**, N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of diphenylureas as RAF kinase inhibitors)  
 RN **284461-42-3** CAPLUS  
 CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN **284461-43-4** CAPLUS  
 CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)

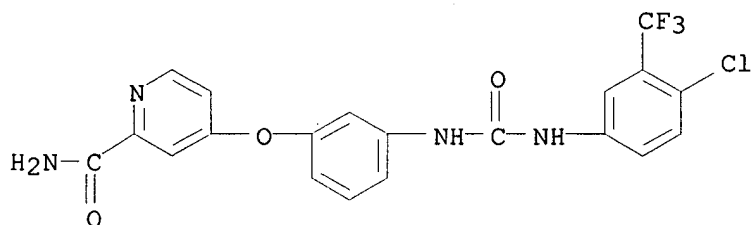


RN **284461-49-0** CAPLUS  
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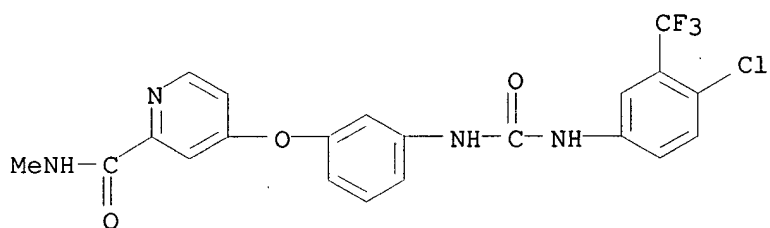
RN **284461-75-2** CAPLUS  
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arbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



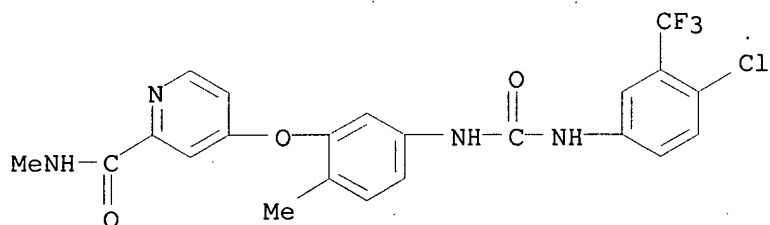
RN 284461-76-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



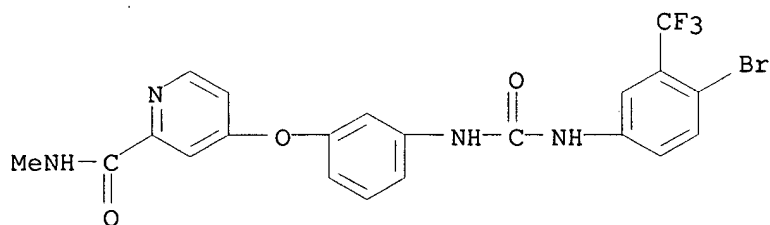
RN 284461-81-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



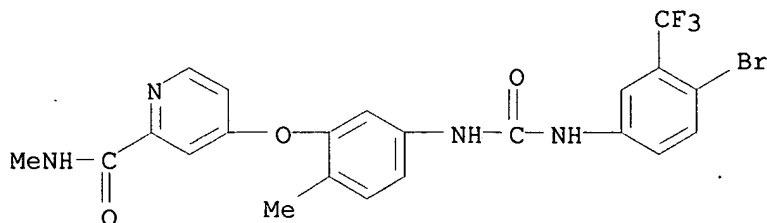
RN 284462-22-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

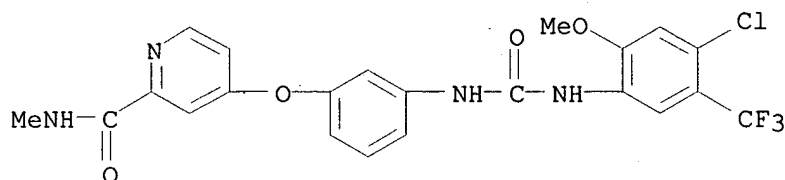


RN 284462-23-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



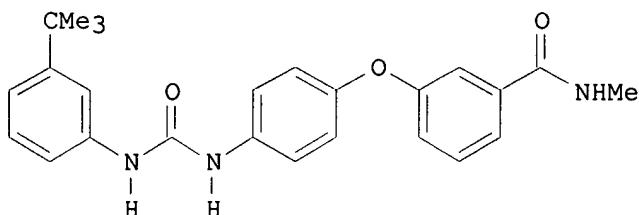
RN 284462-31-3 CAPLUS  
 CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



L125 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4  
 ACCESSION NUMBER: 2002:615574 CAPLUS  
 DOCUMENT NUMBER: 137:169425  
 TITLE: Preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors  
 INVENTOR(S): Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Sibley, Robert N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.  
 PATENT ASSIGNEE(S): Bayer Corporation, USA  
 SOURCE: PCT Int. Appl., 125 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062763	A2	20020815	WO 2002-US3361	20020207
WO 2002062763	A3	20021010		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002165394	A1	20021107	US 2001-777920	20010207
PRIORITY APPLN. INFO.:				
			US 2001-777920	A 20010207
			US 1999-115877P	P 19990113
			US 1999-257266	B2 19990225
			US 1999-425228	B2 19991022
			US 2001-758548	A2 20010112
OTHER SOURCE(S): MARPAT 137:169425				

ED Entered STN: 16 Aug 2002  
GI



AB Title compds., e.g., RNHCONHZOR1 [I; R = C<sub>6</sub>H<sub>4</sub>(CMe<sub>3</sub>)-3, 2-methoxy-5-trifluoromethylphenyl, 4-chloro-3-trifluoromethylphenyl, 2-methoxy-3-quinolyl, etc.; R1 = (un)substituted acylphenyl, -acylpyridinyl, etc.; Z = (un)substituted 1,3- or -1,4-phenylene] were prepd. Thus, 4-(H<sub>2</sub>N)C<sub>6</sub>H<sub>4</sub>OC<sub>6</sub>H<sub>4</sub>(CONHMe)-4 (prepn. given) was condensed with 3-(Me<sub>3</sub>C)C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub> and CO(OCCl<sub>3</sub>)<sub>2</sub> to give title compd. II. Data for biol. activity of title compds. were given.

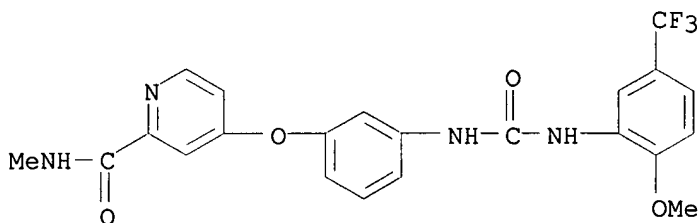
IT 284461-42-3P 284461-43-4P 284461-49-0P  
284461-75-2P 284461-76-3P 284461-81-0P  
284462-22-2P 284462-23-3P 284462-31-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)

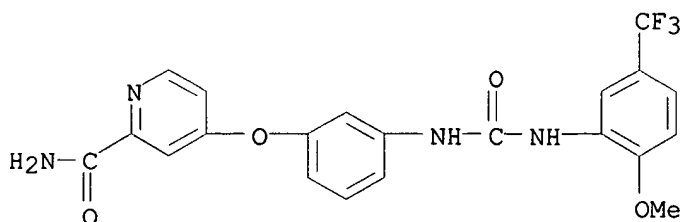
RN 284461-42-3 CAPLUS

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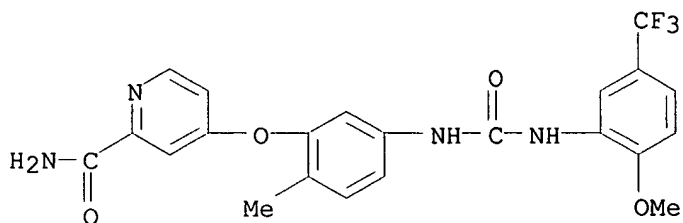
RN 284461-43-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)

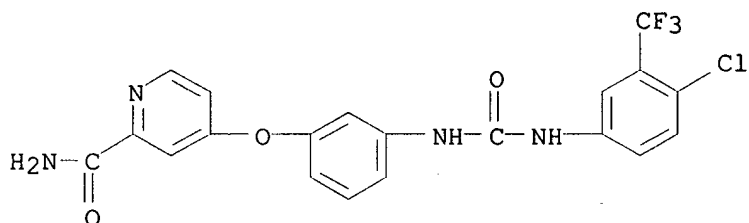


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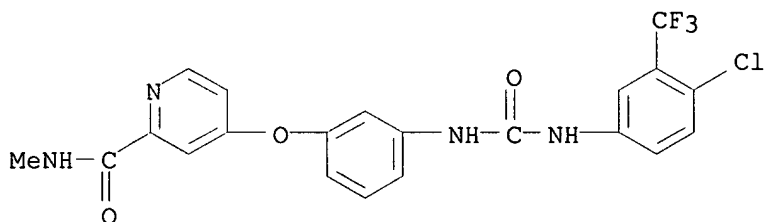
CN 2-Pyridinecarboxamide, 4-[5-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]- (9CI) (CA INDEX NAME)



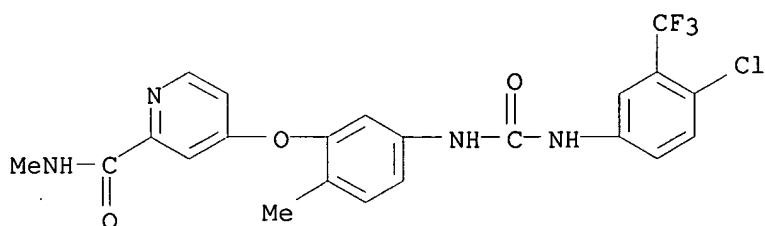
RN 284461-75-2 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



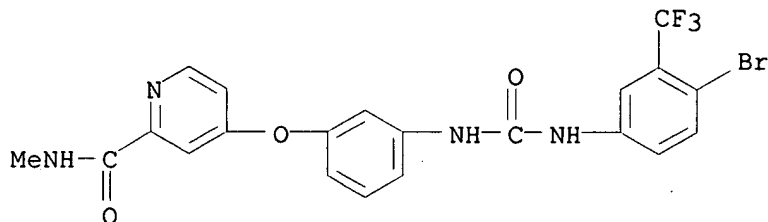
RN 284461-76-3 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-81-0 CAPLUS  
CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)

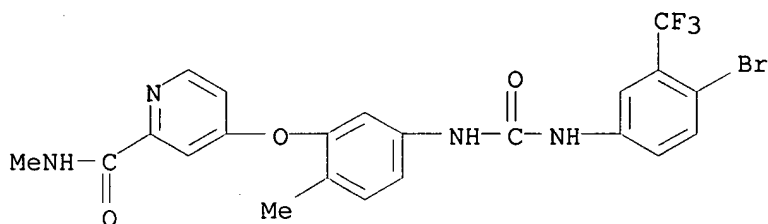


RN 284462-22-2 CAPLUS  
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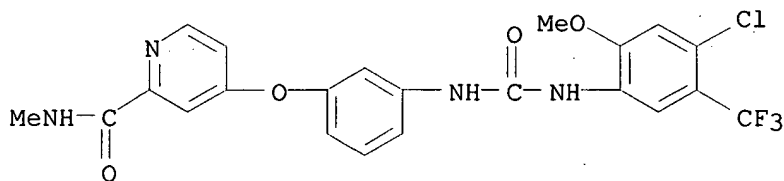
RN 284462-23-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



L125 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2002:850357 CAPLUS

DOCUMENT NUMBER: 137:352907

TITLE: Preparation of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf kinase for the treatment of tumors and/or cancerous cell growth

INVENTOR(S): Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Robert, Sibley N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 63 pp., Cont.-in-part of U.S. Ser. No. 758,548.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2002165394	A1	20021107	US 2001-777920	20010207
ZA 2001005751	A	20030714	ZA 2001-5751	20010712
US 2002137774	A1	20020926	US 2001-907970	20010719
WO 2002062763	A2	20020815	WO 2002-US3361	20020207
WO 2002062763	A3	20021010		

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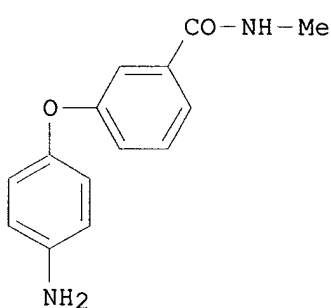
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003139605	A1	20030724	US 2002-71248	20020211
PRIORITY APPLN. INFO.:			US 1999-115877P	P 19990113
			US 1999-257266	B2 19990225
			US 1999-425228	B2 19991022
			US 2001-758548	A2 20010112
			US 1999-115878P	P 19990113
			US 2001-777920	A 20010207
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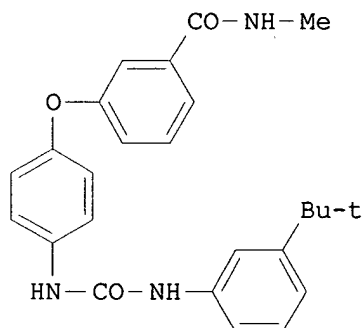
OTHER SOURCE(S): MARPAT 137:352907

ED Entered STN: 08 Nov 2002

GI



II



III

AB Title compds. B-NHCONH-L-(M-L1)<sub>q</sub> (I) [B = (un)substituted pyridyl, quinolinyl, isoquinolinyl; L = 5 or 6 membered cyclic structure; L1 = substituted cyclic moiety having at least 5 members; M = bridging group having at least one atom; q = 1-3; with proviso that L and L1 contain 0-4 hetero atoms, e.g., N, O and S] and their pharmaceutically acceptable salts were prepd. For example, coupling of aniline II, e.g., prepd. from Et 3-hydroxybenzoate in 4-steps, with bis(trichloromethyl)carbonate followed by 3-tert-butylaniline afforded urea III. In in vitro raf kinase assays, 112-specific examples of compds. I inhibited kinase activity with IC50 values ranging from 10 nM-10 .mu.M. Compds. I are useful for the treatment of cancerous cell growth mediated by raf kinase.

IT 284461-42-3P 284461-43-4P 284461-49-0P  
284461-75-2P 284461-76-3P 284461-81-0P  
284462-22-2P 284462-23-3P 284462-31-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

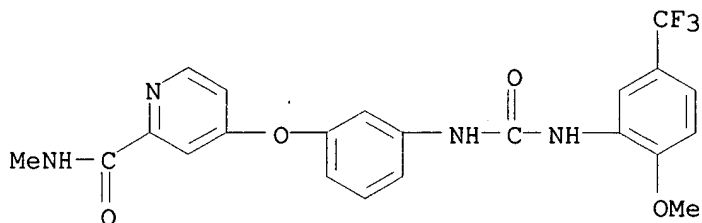
(drug candidate; prepn. of quinolyl, isoquinolyl or pyridyl-ureas as



inhibitors of raf kinase)

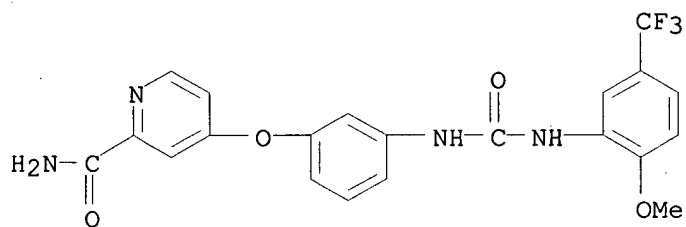
RN 284461-42-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



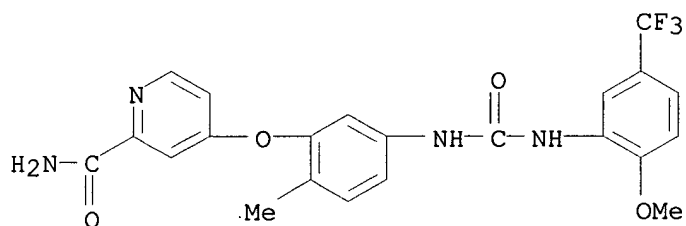
RN 284461-43-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



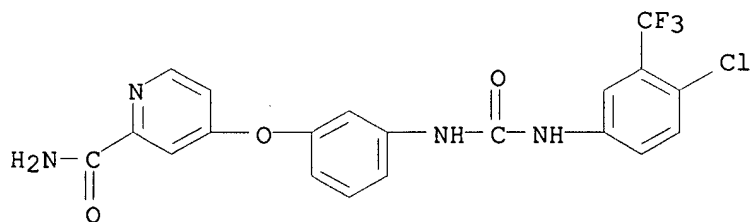
RN 284461-49-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]- (9CI) (CA INDEX NAME)



RN 284461-75-2 CAPLUS

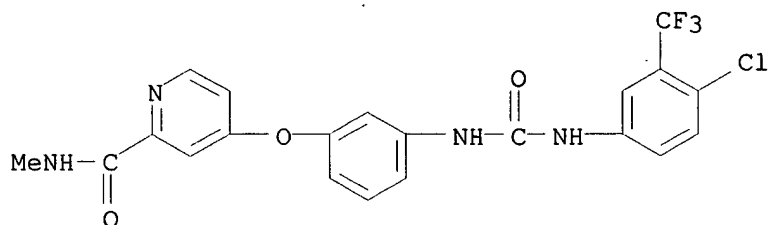
CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



RN 284461-76-3 CAPLUS

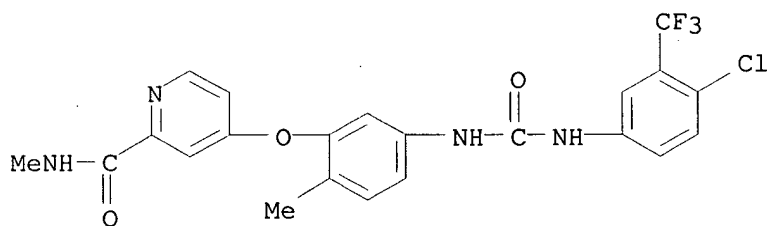
CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)

carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



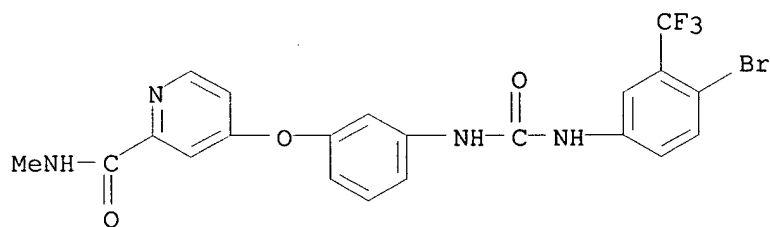
RN 284461-81-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



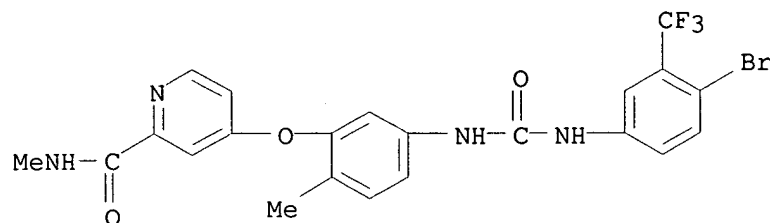
RN 284462-22-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



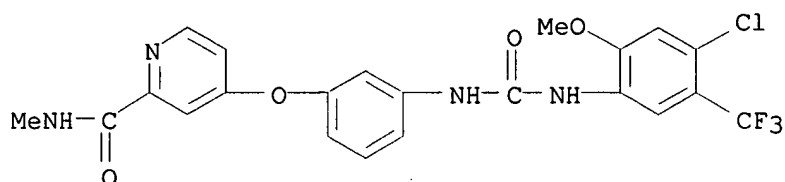
RN 284462-23-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

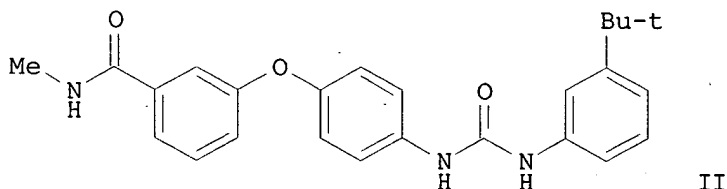


L125 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6  
ACCESSION NUMBER: 2000:493516 CAPLUS  
DOCUMENT NUMBER: 133:120157  
TITLE: Preparation of .omega.-carboxy(hetero)aryl substituted  
diphenyl ureas as raf kinase inhibitors  
INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger,  
Timothy B.; Scott, William J.; Smith, Roger A.; Wood,  
Jill E.; Monahan, Mary-Katherine; Natero, Reina;  
Renick, Joel; Sibley, Robert N.  
PATENT ASSIGNEE(S): Bayer Corporation, USA  
SOURCE: PCT Int. Appl., 120 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 5  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000/42012	A1	20000720	WO 2000-US648	20000112
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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AU 2000025016	A5	20000801	AU 2000-25016	20000112
EP 1140840	A1	20011010	EP 2000-903239	20000112
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US 2001011136	A1	20010802	US 2001-773675	20010202
US 2001016659	A1	20010823	US 2001-773672	20010202
US 2001027202	A1	20011004	US 2001-773658	20010202
US 2001034447	A1	20011025	US 2001-773604	20010202
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US 1999-115878P P 19990113  
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OTHER SOURCE(S): MARPAT 133:120157  
 ED Entered STN: 21 Jul 2000  
 GI



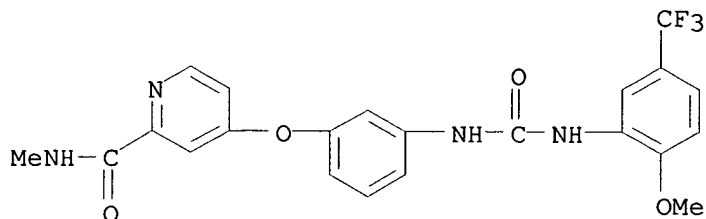
AB This invention relates to the prepn. and use of (hetero)aryl ureas ANHCONHB [I; A = L(ML1)q; L = 5- or 6-membered (hetero)aryl, esp. Ph or pyridinyl; M = bridging group; L1 = (hetero)aryl with at least one (un)substituted sulfamoyl, carboxy, or carbamoyl substituent; q = 1-3; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] for the treatment of raf mediated diseases, such as cancer (no data). Approx. 100 invention compds. and numerous intermediates were prepd. For instance, 3-tert-butyraniline was coupled with bis(trichloromethyl)carbonate to form the isocyanate, followed by addn. of 4-(3-N-methylcarbamoylphenoxy)aniline (prepn. given) to afford the urea II.

IT **284461-42-3P 284461-43-4P**, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea  
**284461-75-2P**, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea **284462-22-2P**, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea **284462-31-3P**, N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[3-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of .omega.-carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

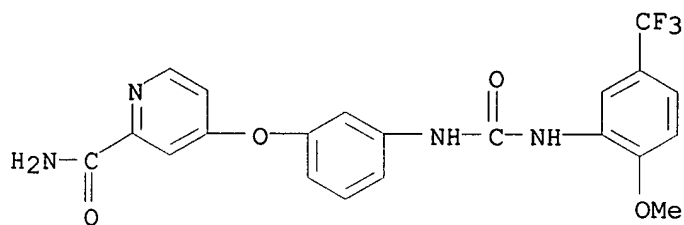
RN 284461-42-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



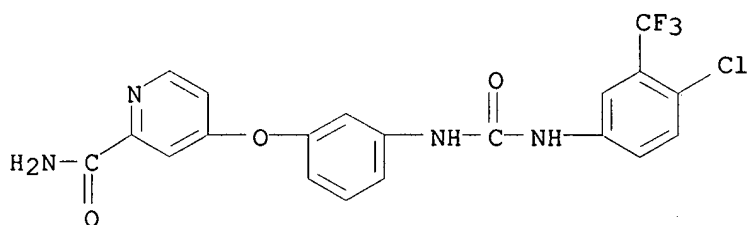
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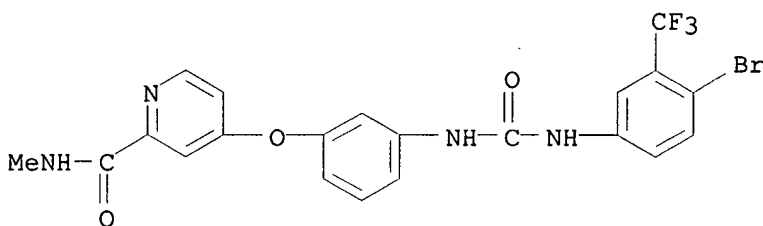
RN 284461-75-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



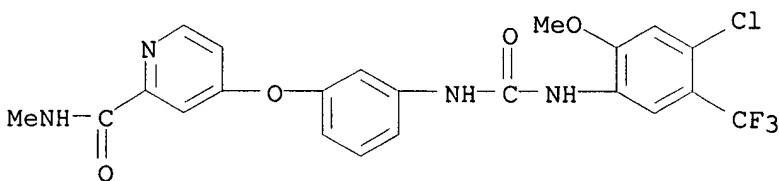
RN 284462-22-2 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



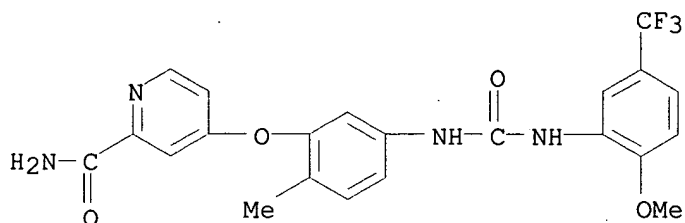
IT 284461-49-0P 284461-81-0P 284462-23-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of .omega.-carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

RN 284461-49-0 CAPLUS

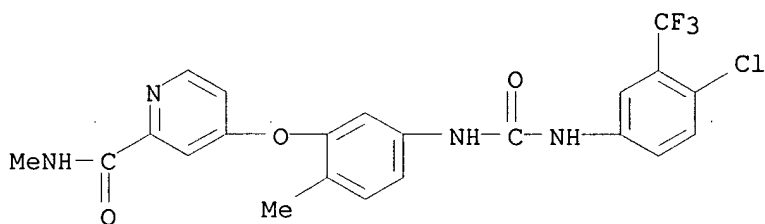
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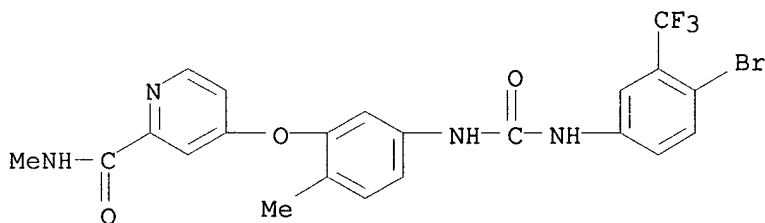
RN 284461-81-0 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-23-3 CAPLUS

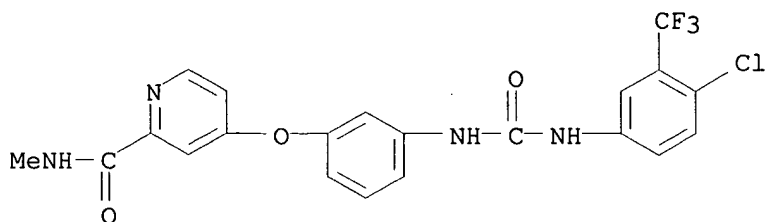
CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



IT **284461-76-3**, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(3-((2-(N-Methylcarbamoyl)-4-pyridyl)oxy)phenyl)urea  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of .omega.-carboxy(hetero)aryl substituted di-Ph urea raf  
kinase inhibitors by reacting arylisocyanates with arylamines)

RN 284461-76-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L125 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:493376 CAPLUS

DOCUMENT NUMBER: 133:120155

TITLE: Preparation of .omega.-carboxy aryl substituted diphenyl ureas as p38 kinase inhibitors

INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 148 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

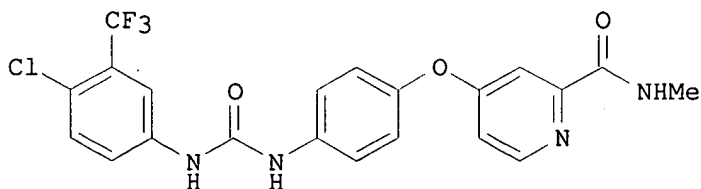
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000041698	A1	20000720	WO 2000-US768	20000113
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2359244	AA	20000720	CA 2000-2359244	20000113
EP 1158985	A1	20011205	EP 2000-905597	20000113
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
US 2003139605	A1	20030724	US 2002-71248	20020211
US 2003105091	A1	20030605	US 2002-86417	20020304
PRIORITY APPLN. INFO.:			US 1999-115878P	P 19990113
			US 1999-257265	A2 19990225
			US 1999-425229	A2 19991022
			US 1999-115877P	P 19990113
			US 1999-257266	B2 19990225
			US 1999-425228	B1 19991022
			WO 2000-US768	W 20000113
			US 2001-948915	A1 20010910

OTHER SOURCE(S): MARPAT 133:120155

ED Entered STN: 21 Jul 2000

GI



II

AB The title compds. ADB [I; D = NHCONH; A = substituted moiety of up to 40 carbon atoms of the formula L(ML1)q (wherein L = 5-6 membered cyclic

structure; L1 = substituted cyclic moiety having at least 5 members; M = bridging group having at least one atom; q = 1-3; each of L and L1 contains 0-4 members of the group consisting of N, O and S); B = (un)substituted up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D contg. 0-4 members of the group consisting of N, O and S], useful in treating p38 mediated diseases, were prepd. E.g., a multi-step synthesis of the urea II which showed IC50 of 1-10 .mu.M against p38, was given. Compds. I are effective at 0.01-200 mg/kg/day (oral administration).

IT 284461-42-3P 284461-43-4P 284461-49-0P

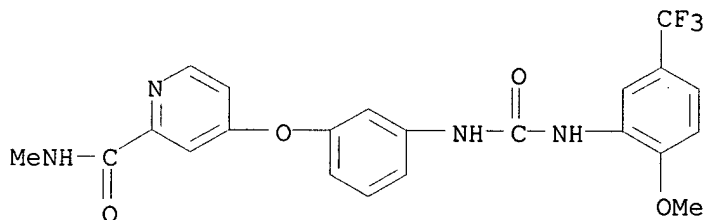
284461-75-2P 284461-76-3P 284461-81-0P

284462-22-2P 284462-23-3P 284462-31-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of .omega.-carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)

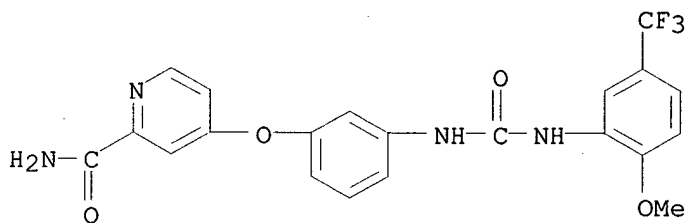
RN 284461-42-3 CAPLUS

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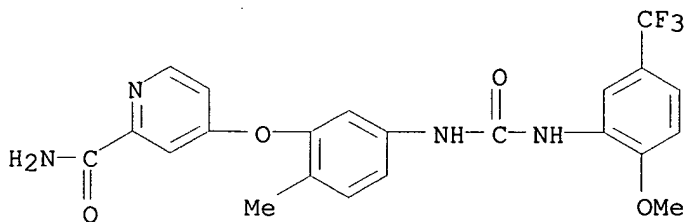
RN 284461-43-4 CAPLUS

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RN 284461-49-0 CAPLUS

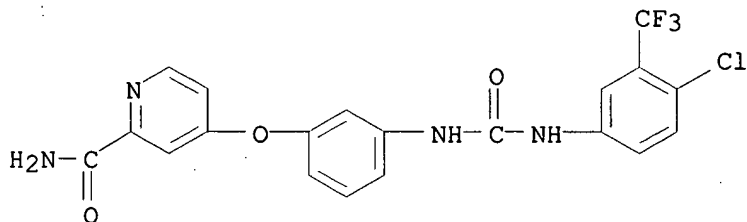
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RN 284461-75-2 CAPLUS

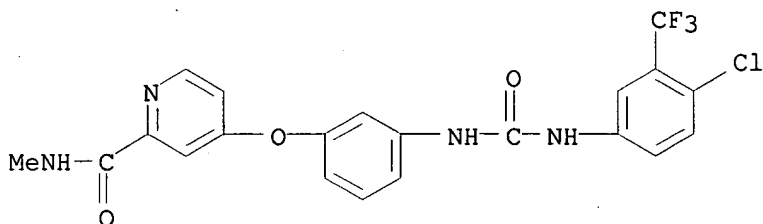


CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



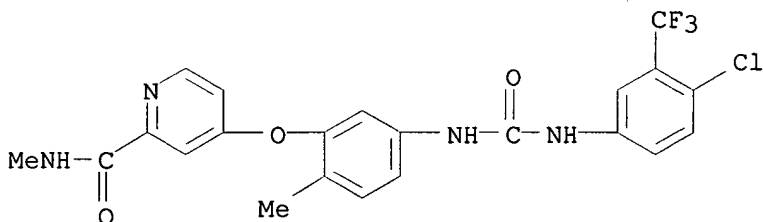
RN 284461-76-3 CAPLUS

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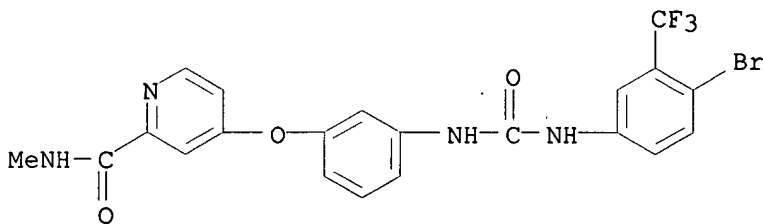
RN 284461-81-0 CAPLUS

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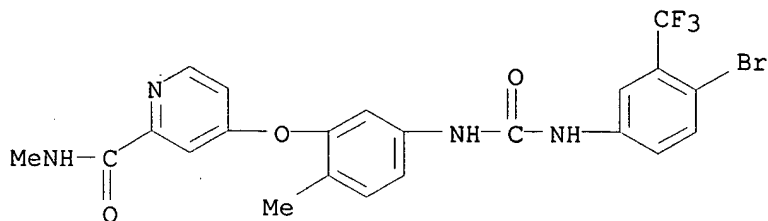
RN 284462-22-2 CAPLUS

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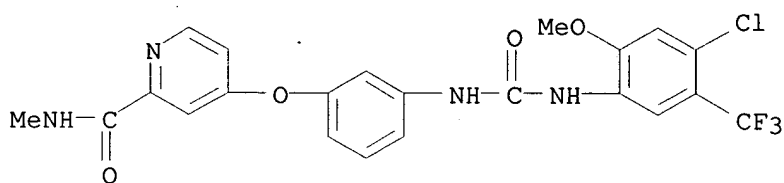
RN 284462-23-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 CAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L125 ANSWER 8 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2003:201617 USPATFULL

TITLE: Method and/or process for preparing omega-carboxyaryl

substituted diphenyl ureas as raf kinas inhibitors

INVENTOR(S): Riedl, Bernd, Wuppertal, GERMANY, FEDERAL REPUBLIC OF

Dumas, Jacques, Bethany, CT, UNITED STATES

Khire, Uday, Hamden, CT, UNITED STATES

Lowinger, Timothy B., Wuppertal, GERMANY, FEDERAL

REPUBLIC OF

Scott, William J., Guilford, CT, UNITED STATES

Smith, Roger A., Madison, CT, UNITED STATES

Wood, Jill E., North Haven, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003139605	A1	20030724
APPLICATION INFO.:	US 2002-71248	A1	20020211 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2001-948915, filed on 10 Sep 2001, PENDING Continuation of Ser. No. US 1999-425228, filed on 22 Oct 1999, ABANDONED Continuation-in-part of Ser. No. US 1999-257266, filed on 25 Feb 1999, ABANDONED		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115877P	19990113 (60)
	US 1999-115878P	19990113 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201	
NUMBER OF CLAIMS:	25	
EXEMPLARY CLAIM:	1	
LINE COUNT:	3287	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to the use of a group of aryl ureas in treating raf mediated diseases, and pharmaceutical compositions for use in such therapy of the formula

A--D--B wherein

D is --NH--C(O)--NH--

A is a substituted moiety of the formula: --L--(M--L.sup.1).sub.q, and

B is a substituted or unsubstituted up to tricyclic aryl or heteroaryl moiety with a t least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen oxygen and sulfur.

L is a 5-6 membered cyclic structure bound directly to D,

L.sup.1 comprises a substituted cyclic moiety having at least 5 members

M is a bridging group having at least one atom and q is an integer of from 1-3.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 284461-42-3P 284461-43-4P 284461-49-0P

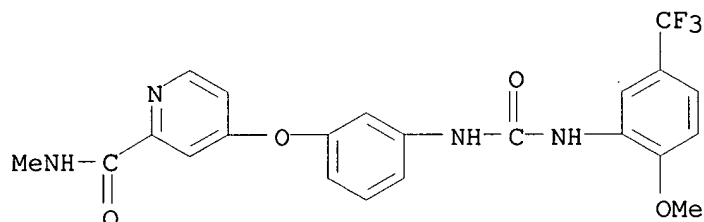
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284462-22-2P 284462-23-3P 284462-31-3P

(prepn. of .omega.-carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)

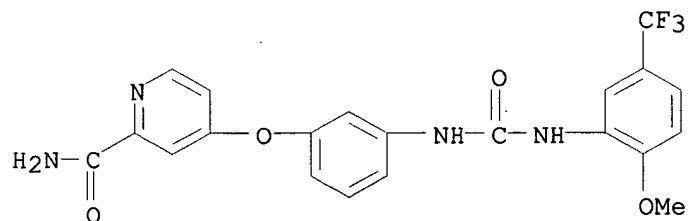
RN 284461-42-3 USPATFULL

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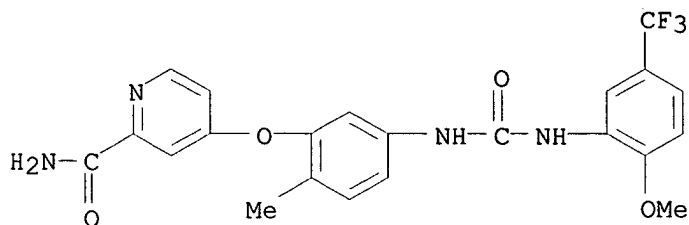
RN 284461-43-4 USPATFULL

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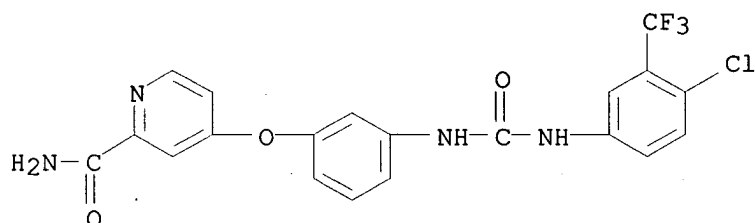
RN 284461-49-0 USPATFULL

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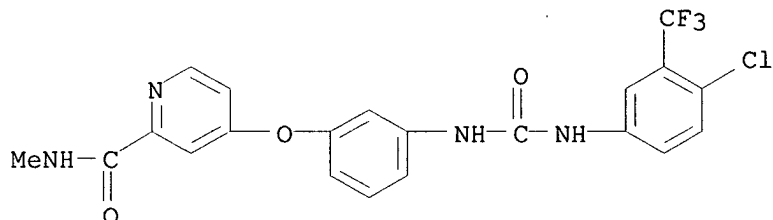
RN 284461-75-2 USPATFULL

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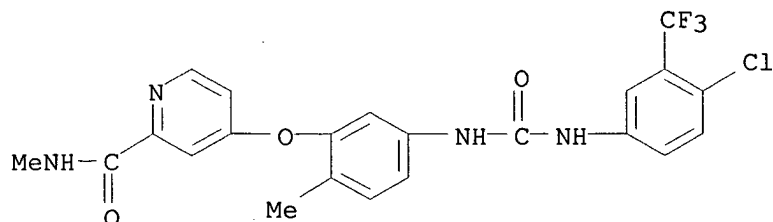
RN 284461-76-3 USPATFULL

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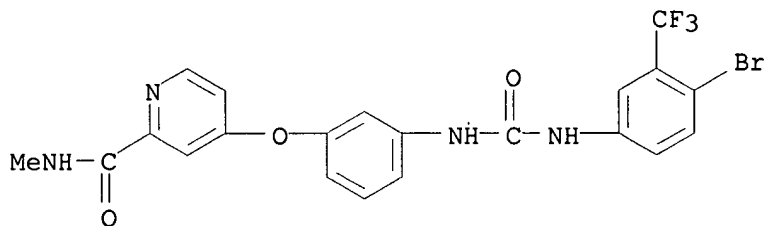
RN 284461-81-0 USPATFULL

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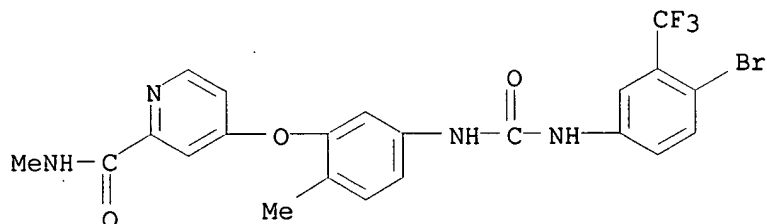
RN 284462-22-2 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



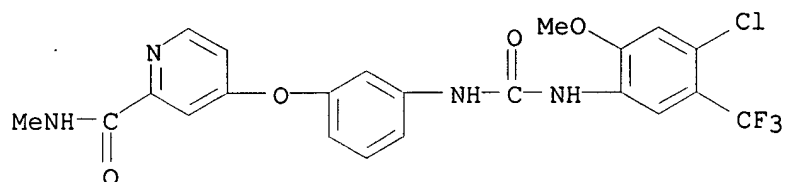
RN 284462-23-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



L125 ANSWER 9 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2003:153423 USPATFULL

TITLE: Omega-carboxy aryl substituted diphenyl ureas as p38 kinase inhibitors

INVENTOR(S): Riedl, Bernd, Wuppertal, GERMANY, FEDERAL REPUBLIC OF  
Dumas, Jacques, Orange, CT, UNITED STATES  
Khire, Uday, Hamden, CT, UNITED STATES  
Lowinger, Timothy B., Nishinomiya, JAPAN  
William, Scott J., Guilford, CT, UNITED STATES  
Smith, Roger A., Madison, CT, UNITED STATES  
Wood, Jill E., Hamden, CT, UNITED STATES  
Monahan, Mary-Katherine, Hamden, CT, UNITED STATES  
Naero, Reina, Hamden, CT, UNITED STATES  
Renick, Joel, Milford, CT, UNITED STATES  
Sibley, Robert N., North Haven, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003105091	A1	20030605
APPLICATION INFO.:	US 2002-86417	A1	20020304 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-425229, filed on 22		

Oct 1999, ABANDONED Continuation-in-part of Ser. No. US  
1999-257265, filed on 25 Feb 1999, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115878P	19990113 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201	
NUMBER OF CLAIMS:	38	
EXEMPLARY CLAIM:	1	
LINE COUNT:	4076	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to the use of a group of aryl ureas in treating  
p38 mediated diseases, and pharmaceutical compositions for use in such  
therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 284461-42-3P 284461-43-4P 284461-49-0P

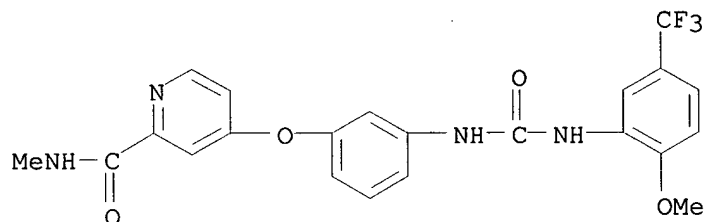
284461-75-2P 284461-76-3P 284461-81-0P

284462-22-2P 284462-23-3P 284462-31-3P

(prepn. of .omega.-carboxy aryl substituted di-Ph ureas as p38 kinase  
inhibitors)

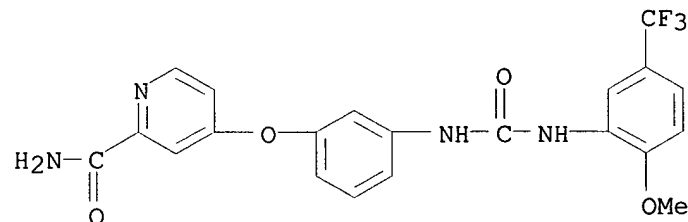
RN 284461-42-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]  
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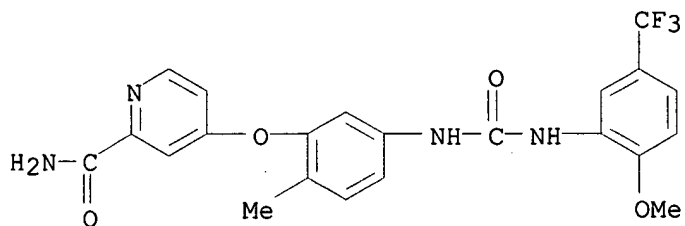
RN 284461-43-4 USPATFULL

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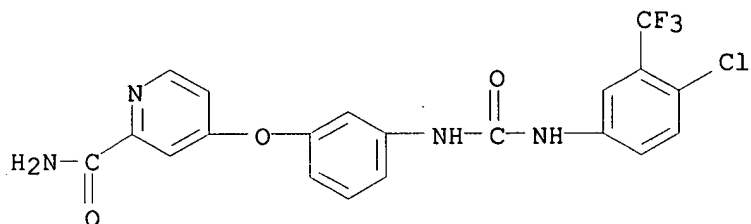
RN 284461-49-0 USPATFULL

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carbonyl]amino]-2-methylphenoxy]- (9CI) (CA INDEX NAME)



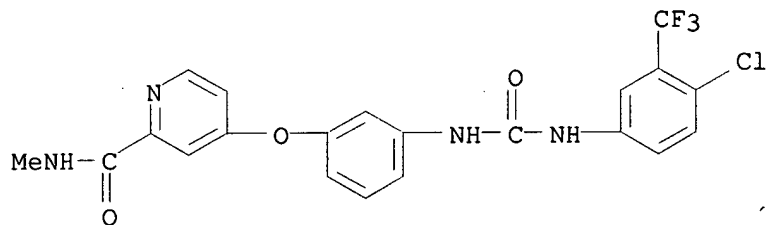
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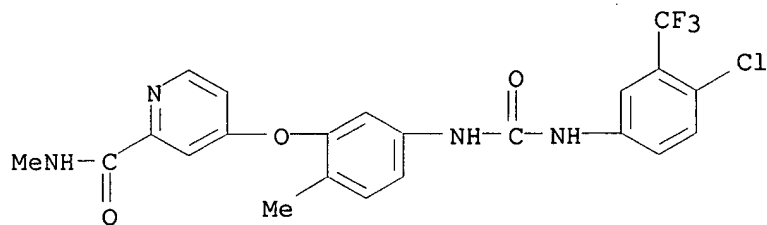
RN 284461-76-3 USPATFULL

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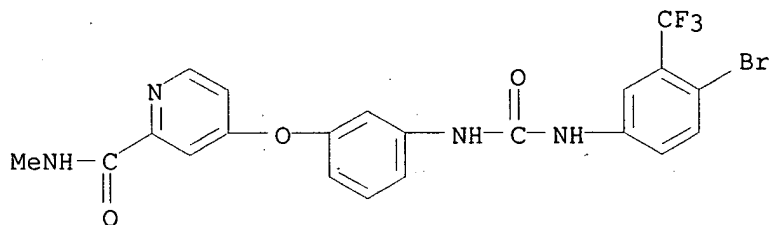
RN 284461-81-0 USPATFULL

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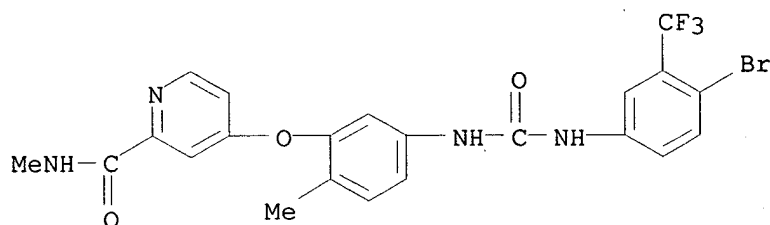
RN 284462-22-2 USPATFULL

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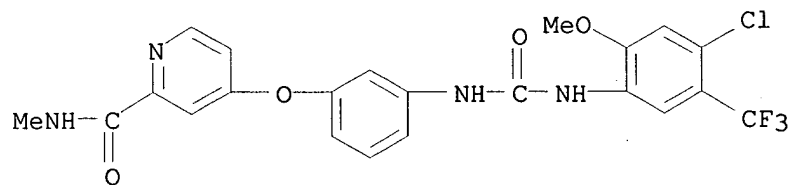
RN 284462-23-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



L125 ANSWER 10 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2002:251820 USPATFULL

TITLE: Carboxyaryl substituted diphenyl ureas as raf kinase inhibitors

INVENTOR(S): Riedl, Bernd, Wuppertal, GERMANY, FEDERAL REPUBLIC OF  
Dumas, Jacques, Orange, CT, UNITED STATES  
Khire, Uday, Hamden, CT, UNITED STATES  
Lowinger, Timothy B., Nishinomiya City, CANADA  
Scott, William J., Guilford, CT, UNITED STATES  
Smith, Roger A., Madison, CT, UNITED STATES  
Wood, Jill E., Hamden, CT, UNITED STATES  
Monahan, Mary-Katherine, Hamden, CT, UNITED STATES  
Natero, Reina, Hamden, CT, UNITED STATES  
Renick, Joel, San Diego, CA, UNITED STATES  
Sibley, Robert N., North Haven, CT, UNITED STATES  
PATENT ASSIGNEE(S): BAYER CORPORATION, Pittsburgh, PA (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002137774	A1	20020926



APPLICATION INFO.: US 2001-907970 A1 20010719 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115877P	19990113 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201	
NUMBER OF CLAIMS:	67	
EXEMPLARY CLAIM:	1	
LINE COUNT:	3732	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

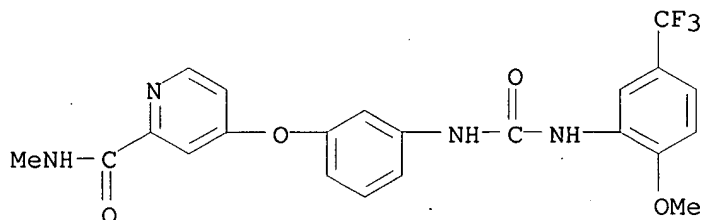
AB This invention relates to the use of a group of aryl ureas in treating raf mediated diseases, and pharmaceutical compositions for use in such therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 284461-42-3P 284461-43-4P 284461-49-0P  
284461-75-2P 284461-76-3P 284461-81-0P  
284462-22-2P 284462-23-3P 284462-31-3P  
(prepn. of .omega.-carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)

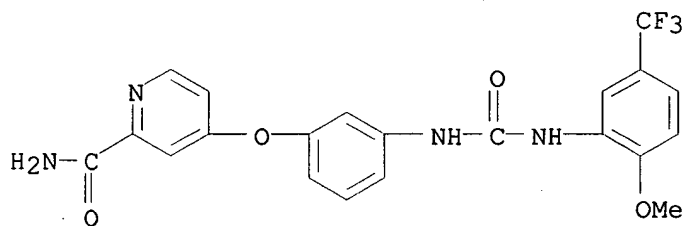
RN 284461-42-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



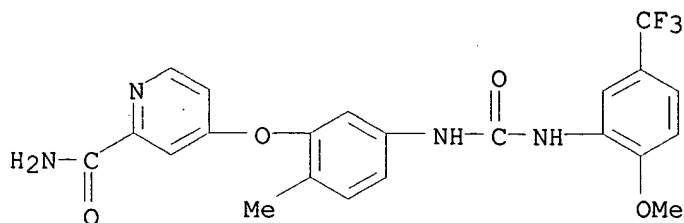
RN 284461-43-4 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



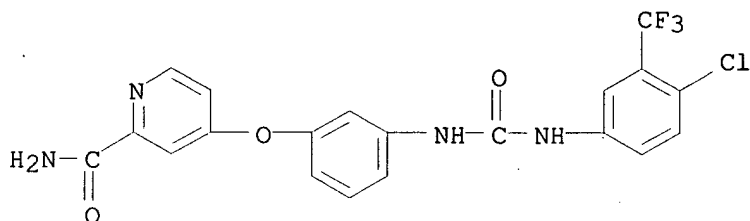
RN 284461-49-0 USPATFULL

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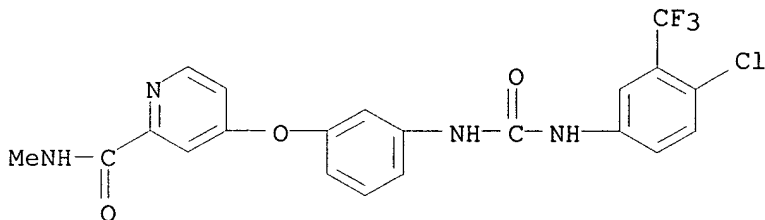
RN 284461-75-2 USPATFULL

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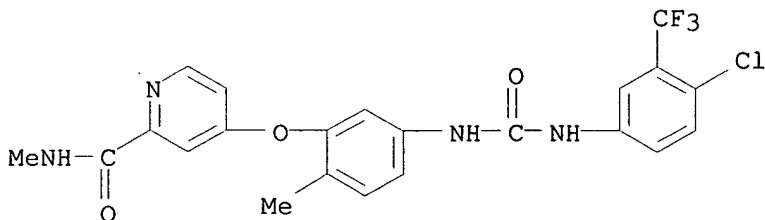
RN 284461-76-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



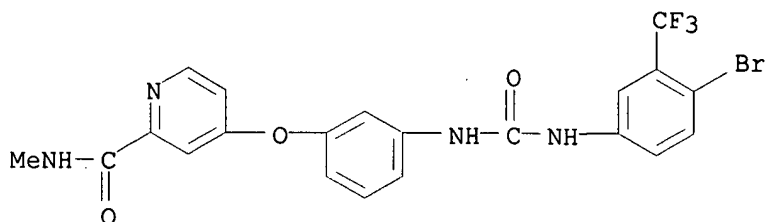
RN 284461-81-0 USPATFULL

CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



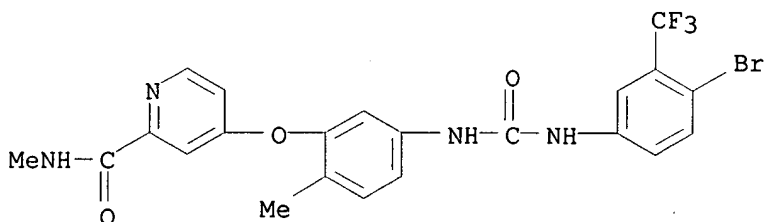
RN 284462-22-2 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



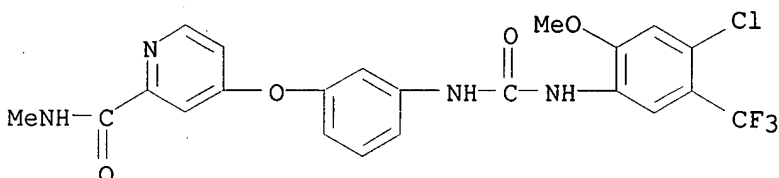
RN 284462-23-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



L125 ANSWER 11 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2002:78859 USPATFULL

TITLE: Omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors

INVENTOR(S): Uday, Khire, Hamden, CT, UNITED STATES  
Dumas, Jacques, Orange, CT, UNITED STATES  
Riedl, Bernd, Wuppertal, GERMANY, FEDERAL REPUBLIC OF  
Lowinger, Timothy B., Nishinomiya City, JAPAN  
Scott, William J., Guilford, CT, UNITED STATES  
Smith, Roger A., Madison, CT, UNITED STATES  
Wood, Jill E., Hamden, CT, UNITED STATES  
Monahan, Mary-Katherine, Hamden, CT, UNITED STATES  
Natero, Reina, Hamden, CT, UNITED STATES  
Joel, Renick, Milford, CT, UNITED STATES  
Sibley, Robert N., North Haven, CT, UNITED STATES

PATENT ASSIGNEE(S): BAYER CORPORATION, Pittsburgh, PA, 15205 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002042517	A1	20020411

APPLICATION INFO.: US 2001-948915 A1 20010910 (9)  
RELATED APPLN. INFO.: Continuation of Ser. No. US 1999-425228, filed on 22  
Oct 1999, ABANDONED Continuation-in-part of Ser. No. US  
1999-257266, filed on 25 Feb 1999, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115877P	19990113 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201	
NUMBER OF CLAIMS:	67	
EXEMPLARY CLAIM:	1	
LINE COUNT:	3675	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

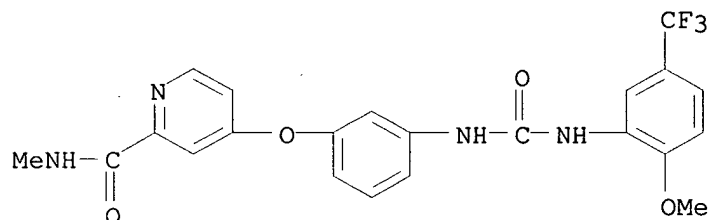
AB This invention relates to the use of a group of aryl ureas in treating raf mediated diseases, and pharmaceutical compositions for use in such therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 284461-42-3P 284461-43-4P 284461-49-0P  
284461-75-2P 284461-76-3P 284461-81-0P  
284462-22-2P 284462-23-3P 284462-31-3P  
(prepn. of .omega.-carboxy aryl substituted di-Ph ureas as p38 kinase  
inhibitors)

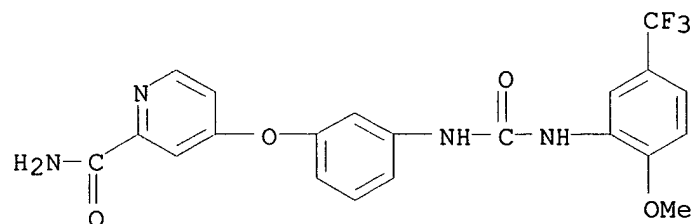
RN 284461-42-3 USPATFULL

2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



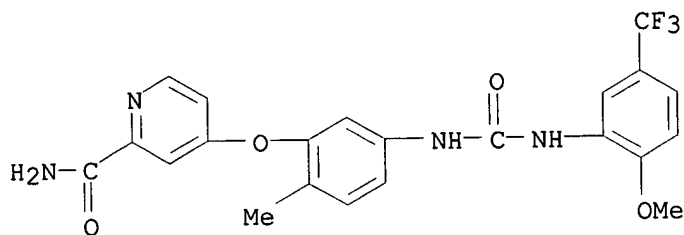
RN 284461-43-4 USPATFULL

2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



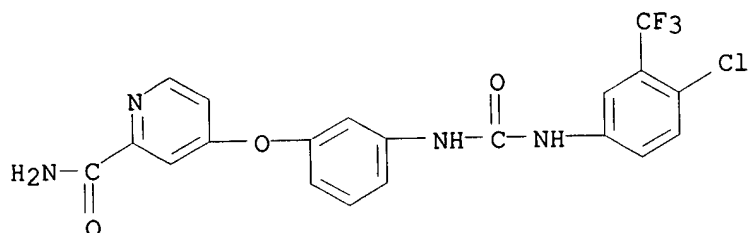
RN 284461-49-0 USPATFULL

2-Pyridinecarboxamide, 4-[5-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]- (9CI) (CA INDEX NAME)



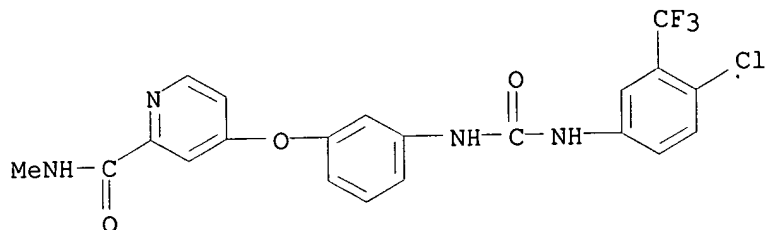
RN 284461-75-2 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



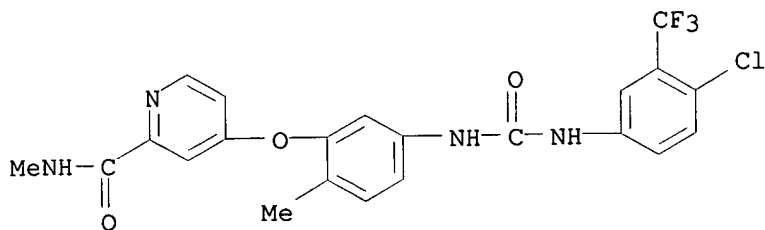
RN 284461-76-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



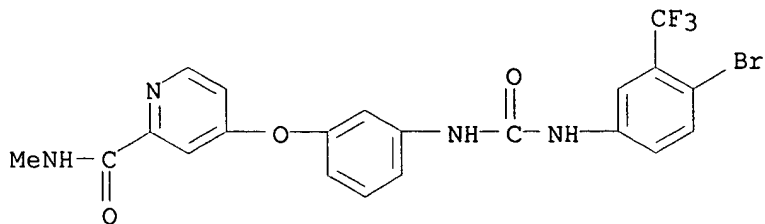
RN 284461-81-0 USPATFULL

CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



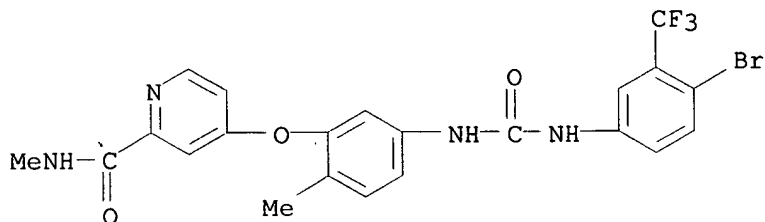
RN 284462-22-2 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



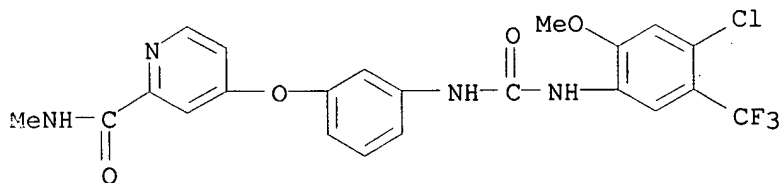
RN 284462-23-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



L12 ANSWER 12 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2001:188813 USPATFULL

TITLE: Omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors

INVENTOR(S): Riedl, Bernd, Wuppertal, Germany, Federal Republic of  
Dumas, Jacques, Orange, CT, United States  
Khire, Uday, Hamden, CT, United States  
Lowinger, Timothy P., Nashnomya City, Japan  
Scott, William J., Guilford, CT, United States  
Smith, Roger A., Madison, CT, United States  
Wood, Jill E., Hamden, CT, United States  
Monahan, Mary-Katherine, Hamden, CT, United States  
Natero, Rena, Hamden, CT, United States  
Renick, Joel, Milford, CT, United States  
Sibley, Robert N., North Haven, CT, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001034447	A1	20011025
APPLICATION INFO.:	US 2001-773604	A1	20010202 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-425228, filed on 22		

Searched by Barb O'Bryen, STIC 571-272-2518

Oct 1999, PENDING Continuation-in-part of Ser. No. US  
1999-257266, filed on 25 Feb 1999, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115877P	19990113 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201	
NUMBER OF CLAIMS:	67	
EXEMPLARY CLAIM:	1	
LINE COUNT:	3666	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

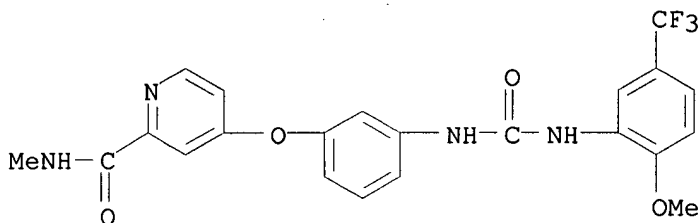
AB This invention relates to the use of a group of aryl ureas in treating  
raf mediated diseases, and pharmaceutical compositions for use in such  
therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 284461-42-3P 284461-43-4P 284461-49-0P  
284461-75-2P 284461-76-3P 284461-81-0P  
284462-22-2P 284462-23-3P 284462-31-3P  
(prepn. of .omega.-carboxy aryl substituted di-Ph ureas as p38 kinase  
inhibitors)

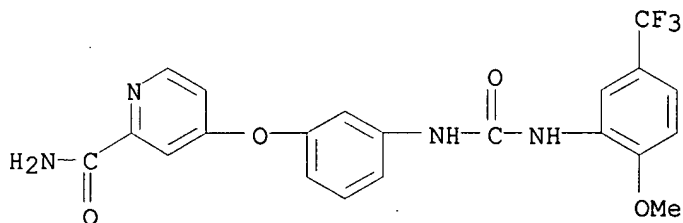
RN 284461-42-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]  
carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



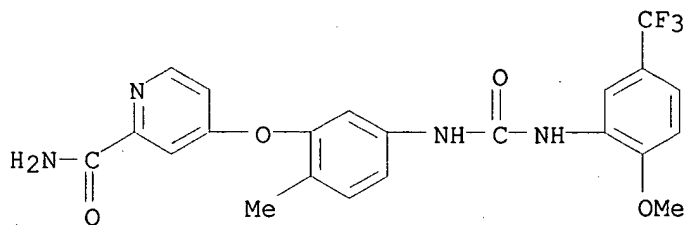
RN 284461-43-4 USPATFULL

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carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



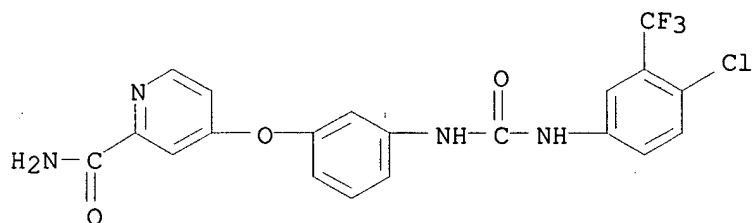
RN 284461-49-0 USPATFULL

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carbonyl]amino]-2-methylphenoxy]- (9CI) (CA INDEX NAME)



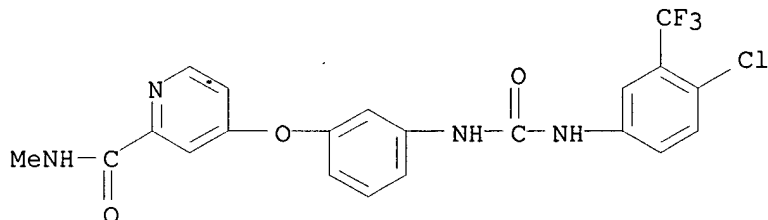
RN 284461-75-2 USPATFULL

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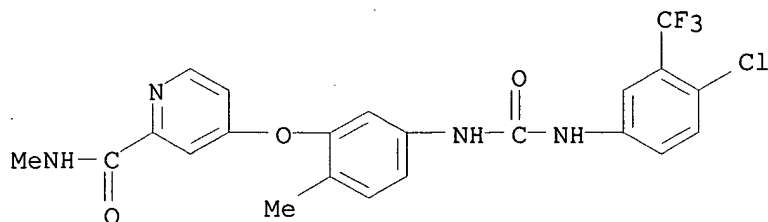
RN 284461-76-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-81-0 USPATFULL

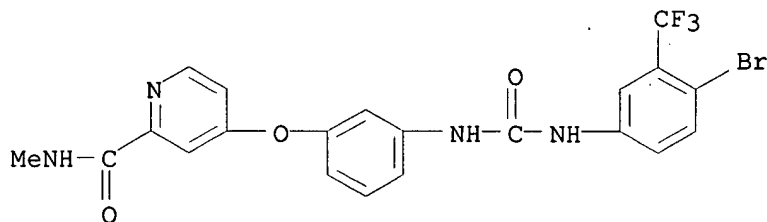
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RN 284462-22-2 USPATFULL

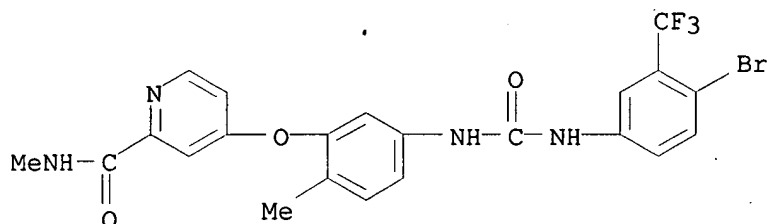
CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)





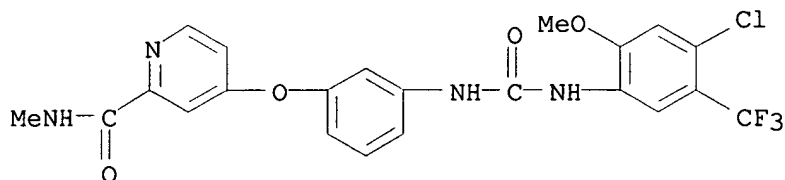
RN 284462-23-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



L125 ANSWER 13 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2001:171152 USPATFULL

TITLE: Omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors

INVENTOR(S): Riedl, Bernd, Wuppertal, Germany, Federal Republic of  
Dumas, Jaques, Orange, CT, United States  
~~Khire, Uday~~, Hamden, CT, United States  
Lowinger, Timothy B., Nishinomiya City, Japan  
Scott, William J., Guilford, CT, United States  
Smith, Roger A., Madison, CT, United States  
Wood, Jill E., Hamden, CT, United States  
Monahan, Mary-Katherine, Hamden, CT, United States  
Natero, Reina, Hamden, CT, United States  
Renick, Joel, Milford, CT, United States  
Sibley, Robert N., Noth Haven, CT, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001027202	A1	20011004
APPLICATION INFO.:	US 2001-773658	A1	20010202 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-425228, filed on 22		

Oct 1999, PENDING Continuation-in-part of Ser. No. US  
1999-257266, filed on 25 Feb 1999, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115877P	19990113 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MILLEN, WHITE, ZELANO & BRANIGAN, P.C., Arlington Courthouse Plaza I, Suite 1400, 2200 Clarendon Boulevard, Arlington, VA, 22201	
NUMBER OF CLAIMS:	67	
EXEMPLARY CLAIM:	1	
LINE COUNT:	3656	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

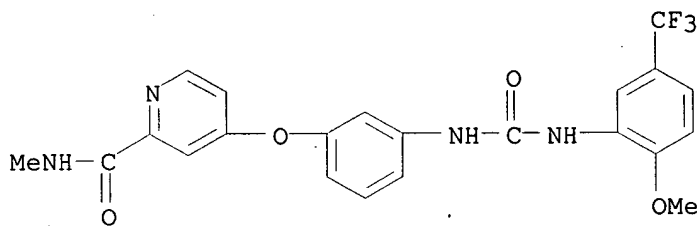
AB This invention relates to the use of a group of aryl ureas in treating  
raf mediated diseases, and pharmaceutical compositions for use in such  
therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 284461-42-3P 284461-43-4P 284461-49-0P  
284461-75-2P 284461-76-3P 284461-81-0P  
284462-22-2P 284462-23-3P 284462-31-3P  
(prepn. of .omega.-carboxy aryl substituted di-Ph ureas as p38 kinase  
inhibitors)

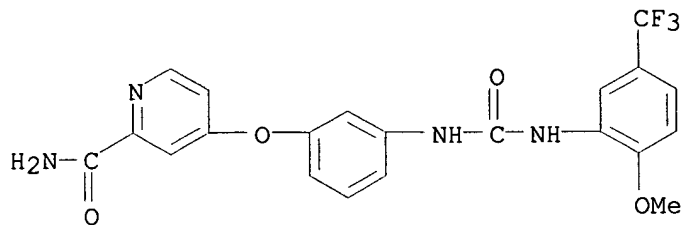
RN 284461-42-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]  
carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



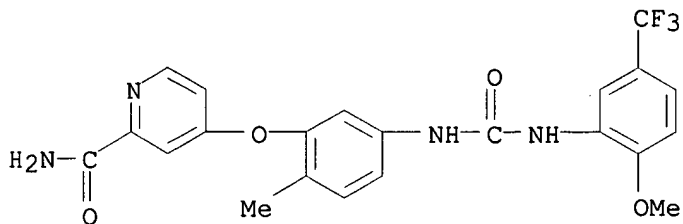
RN 284461-43-4 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]  
carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



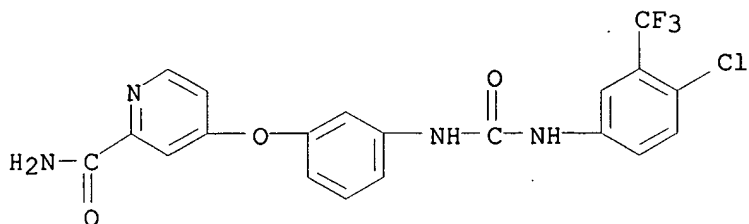
RN 284461-49-0 USPATFULL

CN 2-Pyridinecarboxamide, 4-[5-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]  
carbonyl]amino]-2-methylphenoxy]- (9CI) (CA INDEX NAME)



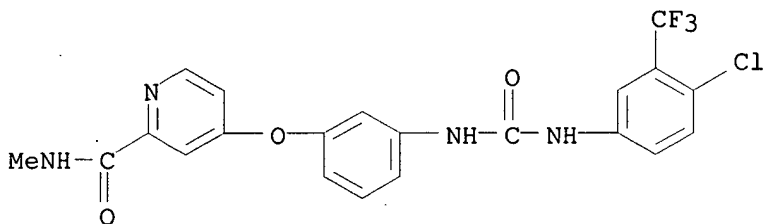
RN 284461-75-2 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



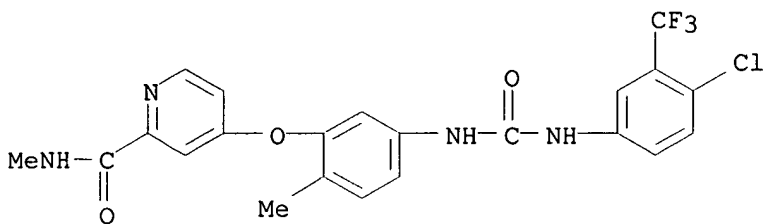
RN 284461-76-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



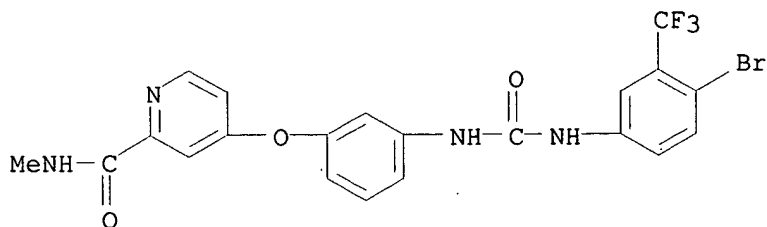
RN 284461-81-0 USPATFULL

CN 2-Pyridinecarboxamide, 4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



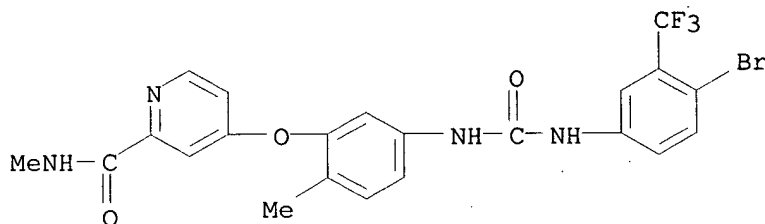
RN 284462-22-2 USPATFULL

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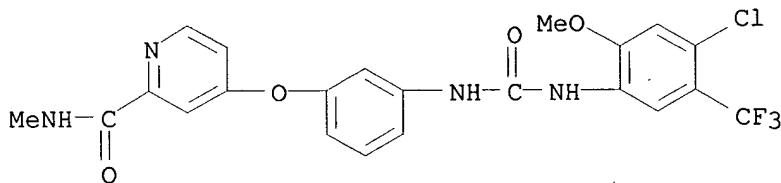
RN 284462-23-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



L125 ANSWER 14 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2001:139616 USPATFULL

TITLE: Omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors

INVENTOR(S): Riedl, Bernd, Wuppertal, Germany, Federal Republic of  
Dumas, Jacques, Orange, CT, United States  
Khire, Uday, Hamden, CT, United States  
Lowinger, Timothy B., Nashnomya City, Japan  
Scott, William J., Guilford, CT, United States  
Smith, Roger A., Madison, CT, United States  
Wood, Jill E., Hamden, CT, United States  
Monahan, Mary-Katherine, Hamden, CT, United States  
Natero, Rena, Hamden, CT, United States  
Renick, Joel, Milford, CT, United States  
Sibley, Robert N., North Haven, CT, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001016659	A1	20010823
APPLICATION INFO.:	US 2001-773672	A1	20010202 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-425228, filed on 22		

Oct 1999, PENDING Continuation-in-part of Ser. No. US  
1999-257266, filed on 25 Feb 1999, ABANDONED

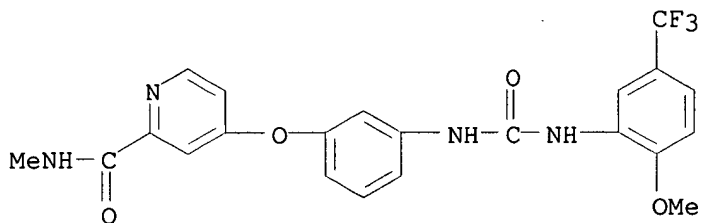
	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115877P	19990113 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201	
NUMBER OF CLAIMS:	67	
EXEMPLARY CLAIM:	1	
LINE COUNT:	3652	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

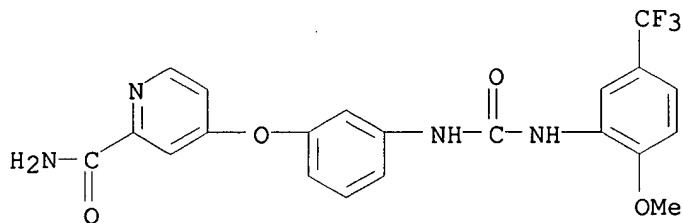
AB This invention relates to the use of a group of aryl ureas in treating  
raf mediated diseases, and pharmaceutical compositions for use in such  
therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

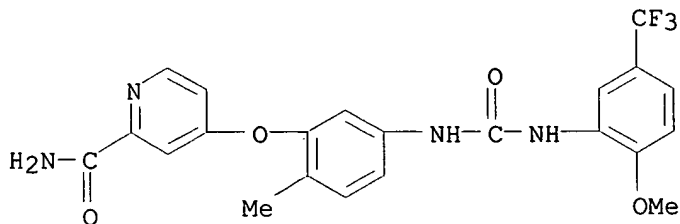
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284461-75-2P 284461-76-3P 284461-81-0P  
284462-22-2P 284462-23-3P 284462-31-3P  
(prepn. of .omega.-carboxy aryl substituted di-Ph ureas as p38 kinase  
inhibitors)  
RN 284461-42-3 USPATFULL  
CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]  
carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284461-43-4 USPATFULL  
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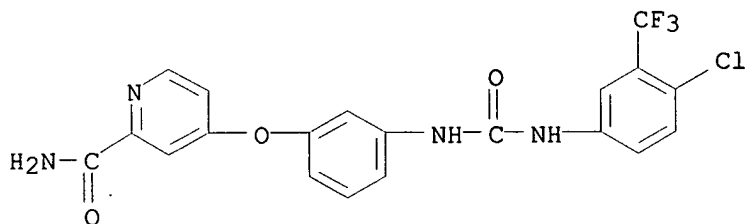


RN 284461-49-0 USPATFULL  
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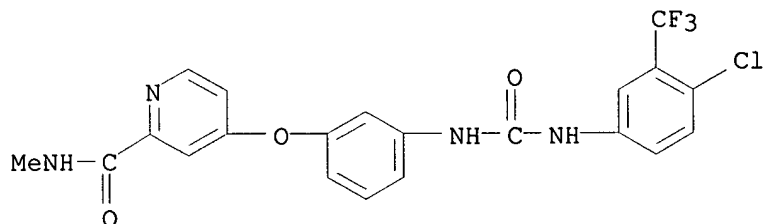
RN 284461-75-2 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



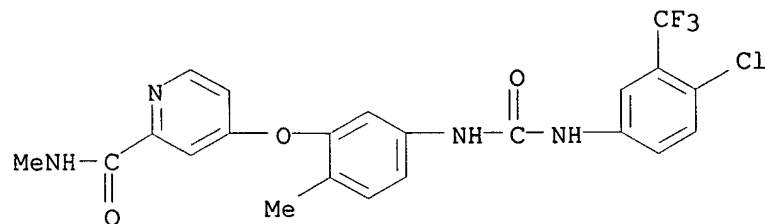
RN 284461-76-3 USPATFULL

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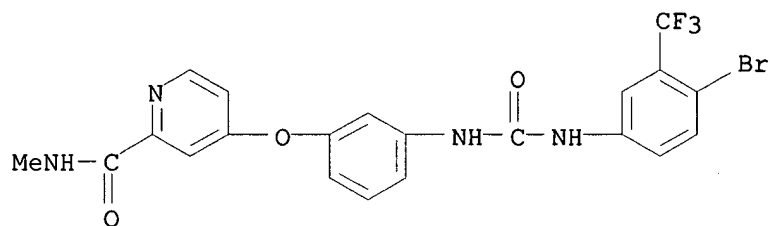
RN 284461-81-0 USPATFULL

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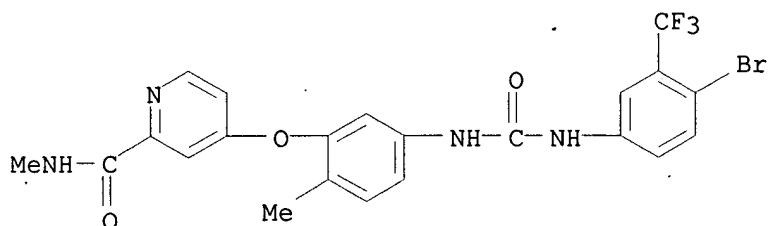
RN 284462-22-2 USPATFULL

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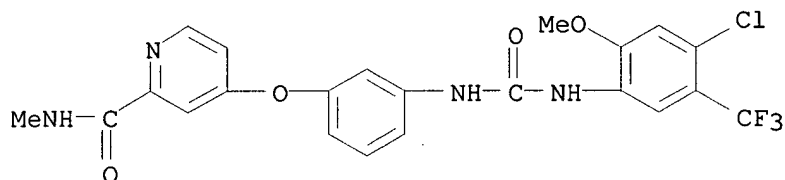
RN 284462-23-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



L125 ANSWER 15 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2001:123628 USPATFULL

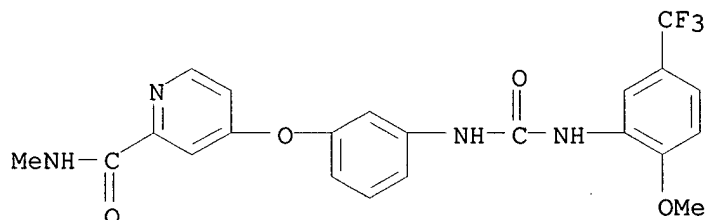
TITLE: omega-carboxyyaryl substituted diphenyl ureas as raf kinase inhibitors

INVENTOR(S): Riedl, Bernd, Wuppertal, Germany, Federal Republic of  
Dumas, Jacques, Orange, CT, United States  
Khire, Uday, Hamden, CT, United States  
Lowinger, Timothy B., Nishinomiya City, Japan  
Scott, William J., Guilford, CT, United States  
Smith, Roger A., Madison, CT, United States  
Wood, Jill E., Hamden, CT, United States  
Monahan, Mary-Katherine, Hamden, CT, United States  
Natero, Reina, Hamden, CT, United States  
Renick, Joel, Milford, CT, United States  
Sibley, Robert N., North Haven, CT, United States

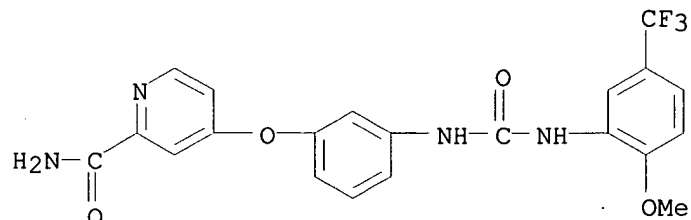
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001011136	A1	20010802
APPLICATION INFO.:	US 2001-773675	A1	20010202 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-425228, filed on 22		

Oct 1999, PENDING Continuation-in-part of Ser. No. US  
1999-257266, filed on 25 Feb 1999, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115877P	19990113 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MILLEN, WHITE, ZELANO & BRANIGAN, P.C., Suite 1400, 2200 Clarendon Blvd., Arlington, VA, 22201	
NUMBER OF CLAIMS:	67	
EXEMPLARY CLAIM:	1	
LINE COUNT:	3646	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
AB	This invention relates to the use of a group of aryl ureas in treating raf mediated diseases, and pharmaceutical compositions for use in such therapy.	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
IT	284461-42-3P 284461-43-4P 284461-49-0P 284461-75-2P 284461-76-3P 284461-81-0P 284462-22-2P 284462-23-3P 284462-31-3P (prepn. of .omega.-carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)	
RN	284461-42-3 USPATFULL	
CN	2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino] carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)	

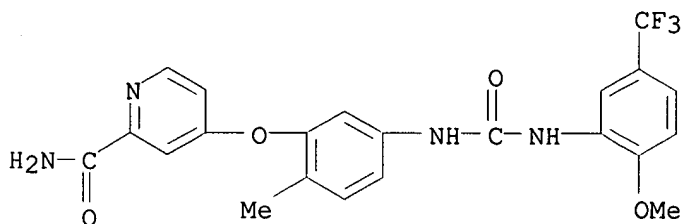


RN 284461-43-4 USPATFULL  
CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]  
carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



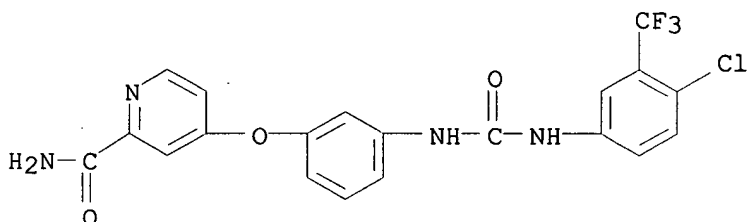
RN 284461-49-0 USPATFULL  
CN 2-Pyridinecarboxamide, 4-[5-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]  
carbonyl]amino]-2-methylphenoxy]- (9CI) (CA INDEX NAME)





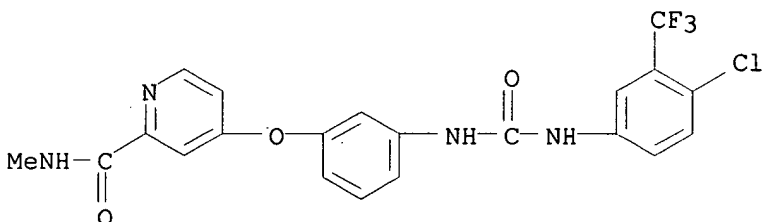
RN 284461-75-2 USPATFULL

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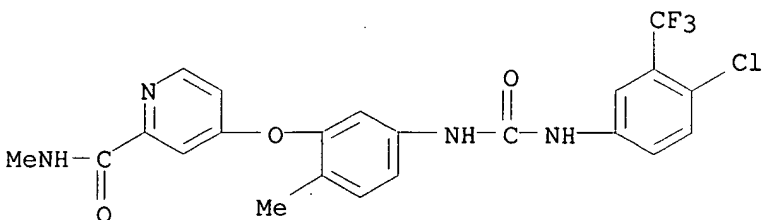
RN 284461-76-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



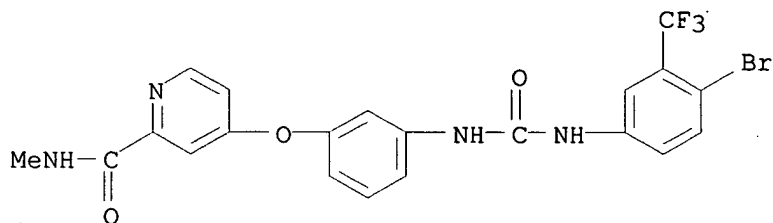
RN 284461-81-0 USPATFULL

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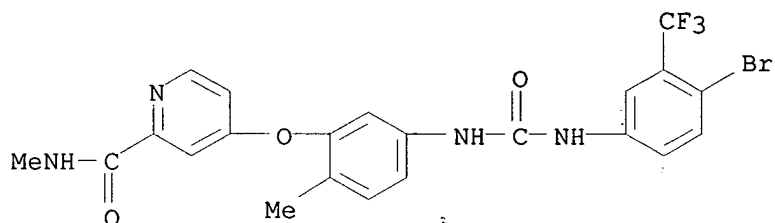
RN 284462-22-2 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



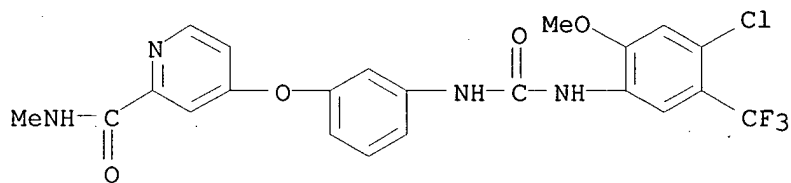
RN 284462-23-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



L125 ANSWER 16 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2001:123627 USPATFULL

TITLE: Omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors

INVENTOR(S): Riedl, Bernd, Wuppertal, Germany, Federal Republic of  
Dumas, Jacques, Orange, CT, United States  
Khire, Uday, Hamden, CT, United States  
Lowinger, Timothy B., Nishinomiya City, Japan  
Scott, William J., Guilford, CT, United States  
Smith, Roger A., Madison, CT, United States  
Wood, Jill E., Hamden, CT, United States  
Monahan, Mary-Katherine, Hamden, CT, United States  
Natero, Reina, Hamden, CT, United States  
Renick, Joel, Milford, CT, United States  
Sibley, Robert N., North Haven, CT, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001011135	A1	20010802
APPLICATION INFO.:	US 2001-773659	A1	20010202 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-425228, filed on 22		

Oct 1999, PENDING Continuation-in-part of Ser. No. US  
1999-257266, filed on 25 Feb 1999, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115877P	19990113 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MILLEN, WHITE, ZELANO & BRANIGAN, P.C., Suite 1400, Arlington Courthouse Plaza 1, Arlington, VA, 22201	
NUMBER OF CLAIMS:	67	
EXEMPLARY CLAIM:	1	
LINE COUNT:	3686	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

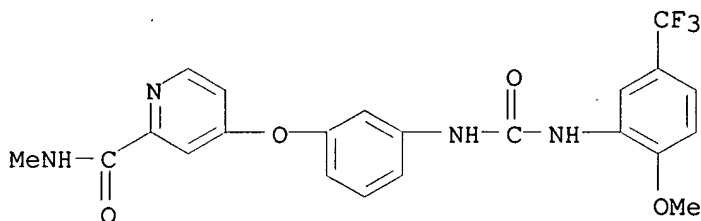
AB This invention relates to the use of a group of aryl ureas in treating  
raf mediated diseases, and pharmaceutical compositions for use in such  
therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 284461-42-3P 284461-43-4P 284461-49-0P  
284461-75-2P 284461-76-3P 284461-81-0P  
284462-22-2P 284462-23-3P 284462-31-3P  
(prepn. of .omega.-carboxy aryl substituted di-Ph ureas as p38 kinase  
inhibitors)

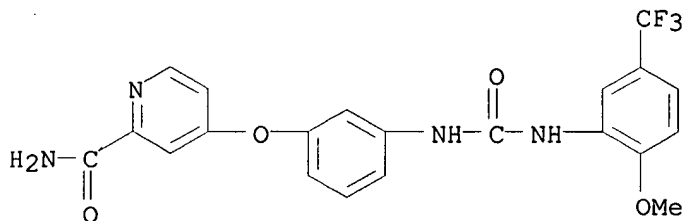
RN 284461-42-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]  
carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



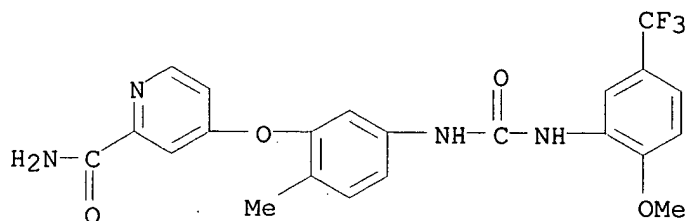
RN 284461-43-4 USPATFULL

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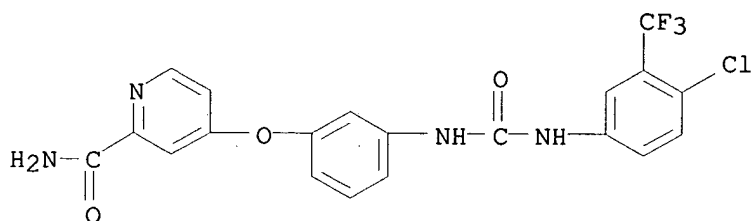
RN 284461-49-0 USPATFULL

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carbonyl]amino]-2-methylphenoxy]- (9CI) (CA INDEX NAME)



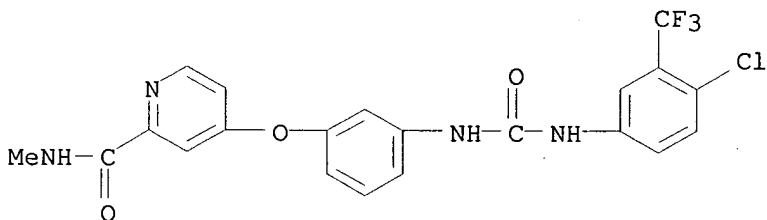
RN 284461-75-2 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



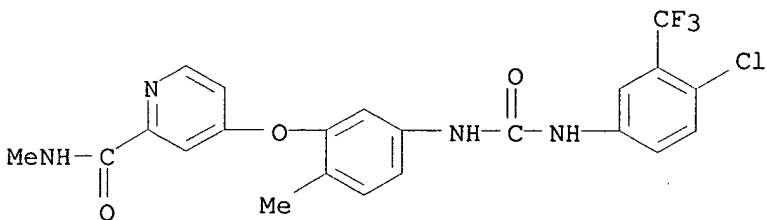
RN 284461-76-3 USPATFULL

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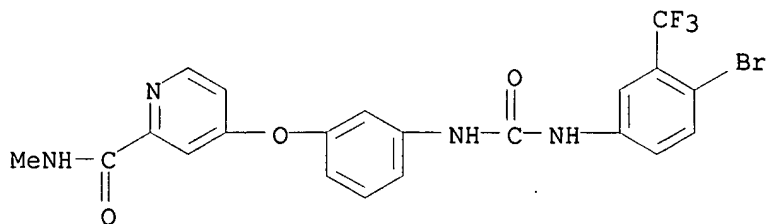
RN 284461-81-0 USPATFULL

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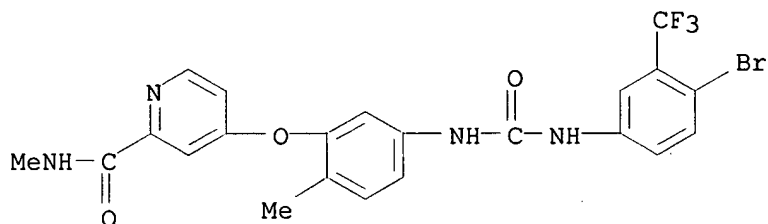
RN 284462-22-2 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



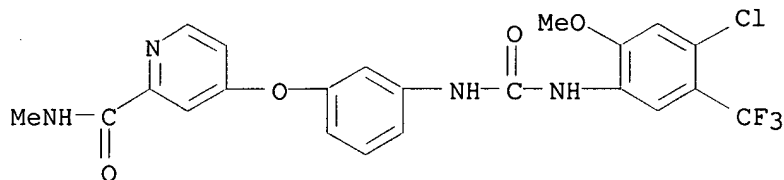
RN 284462-23-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[5-[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-2-methylphenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 284462-31-3 USPATFULL

CN 2-Pyridinecarboxamide, 4-[3-[[[4-chloro-2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



FILE 'HOME' ENTERED AT 17:02:16 ON 09 MAR 2004



blockage of EGF signal transduction.

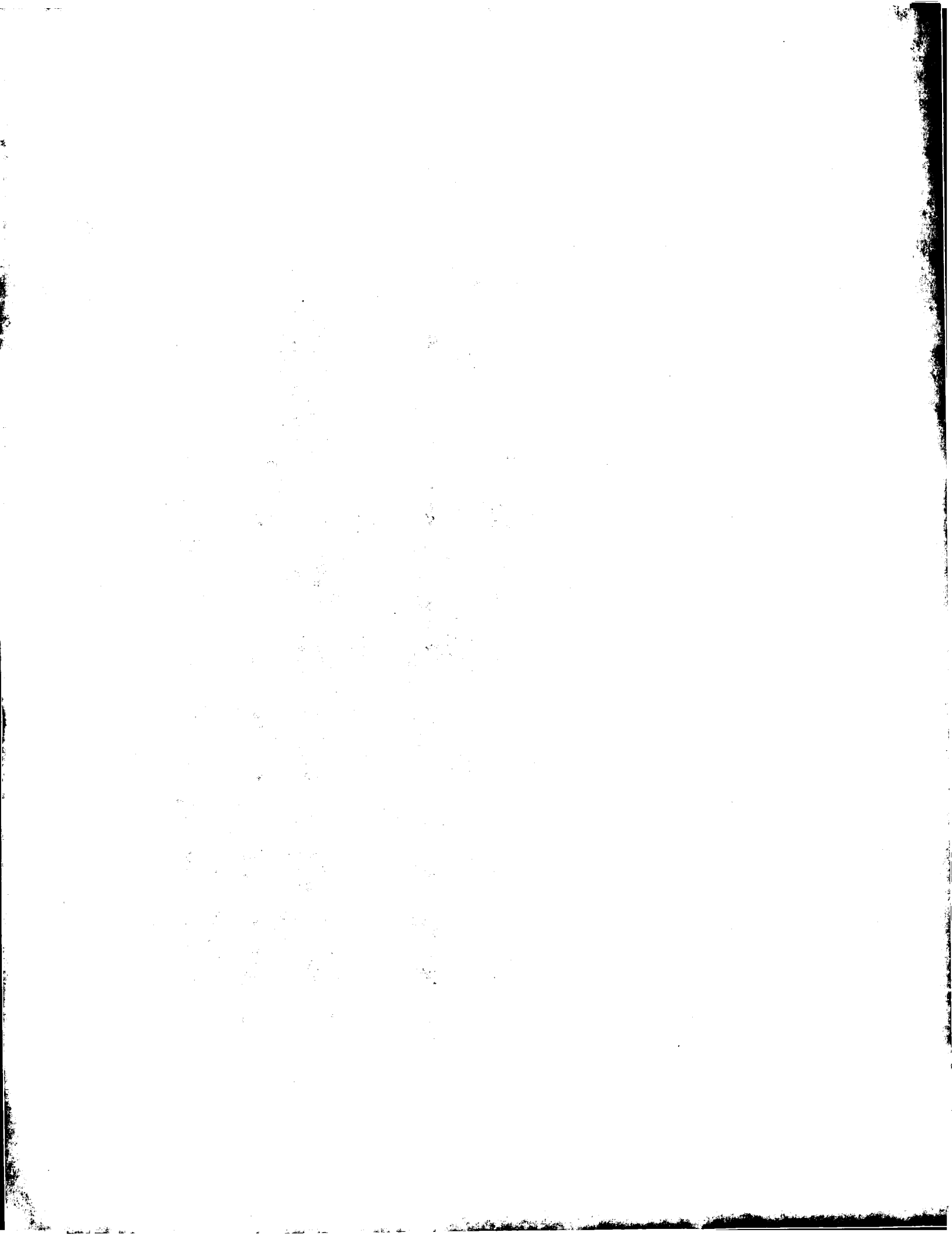
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Blotting, Northern  
\*Carcinoma, Non-Small-Cell Lung: DT, drug therapy  
\*Carcinoma, Non-Small-Cell Lung: ME, metabolism  
Cell Division: DE, drug effects  
\*Gene Expression Regulation, Neoplastic: DE, drug effects  
Genes, fos  
Genes, myc  
\*Lung Neoplasms: DT, drug therapy  
\*Lung Neoplasms: ME, metabolism  
RNA, Messenger: ME, metabolism  
RNA, Neoplasm: ME, metabolism  
\*Receptor, Epidermal Growth Factor: BI, biosynthesis  
Receptor, Epidermal Growth Factor: ME, metabolism  
\*Suramin: PD, pharmacology  
Tumor Cells, Cultured  
CAS REGISTRY NO.: 145-63-1 (Suramin)  
CHEMICAL NAME: 0 (Anticarcinogenic Agents); 0 (RNA, Messenger); 0 (RNA, Neoplasm); EC 2.7.1.112 (Receptor, Epidermal Growth Factor)

L122 ANSWER 25 OF 28 MEDLINE on STN DUPLICATE 6  
ACCESSION NUMBER: 96336811 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8738403  
TITLE: Intravesical suramin: a novel agent for the treatment of superficial transitional-cell carcinoma of the bladder.  
AUTHOR: Walther M M; Figg W D; Linehan W M  
CORPORATE SOURCE: Urologic Oncology Section, National Cancer Institute, Bethesda, MD 20892, USA.  
SOURCE: World journal of urology, (1996) 14 Suppl 1 S8-11. Ref: 31  
Journal code: 8307716. ISSN: 0724-4983.  
PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199612  
ENTRY DATE: Entered STN: 19970128  
Last Updated on STN: 19970128  
Entered Medline: 19961202

ABSTRACT:

Patients with recurrent or high-grade superficial transitional-cell carcinoma of the **bladder** that has recurred after intravesical chemotherapy are at increased risk for tumor invasion and metastases. Intravesical chemotherapy is a minimally invasive technique that allows high doses of therapeutic agents to be delivered directly to the malignancy, doses that would not be tolerated systemically. In vitro studies demonstrate suramin's significant efficacy against transitional-cell carcinoma cell lines at relatively low doses. Humans treated with similar doses delivered in a systemic fashion have experienced no \*\*\*bladder\*\*\* toxicity. Suramin has been shown to block the binding of epidermal growth factor (EGF) to its receptors, which are found in large amounts in **bladder** cancers. Because a significant association has been found between the number of EGF receptors on a **bladder-cancer** cell and its sensitivity to suramin, transitional-cell carcinoma could potentially be very responsive to such therapy. On the basis of these findings, a phase I escalating-suramin-dose study is currently being conducted.

CONTROLLED TERM: Check Tags: Human  
Administration, Intravesical  
Animals  
Antineoplastic Agents: AD, administration & dosage





\*Antineoplastic Agents: TU, therapeutic use  
\*Bladder Neoplasms: DT, drug therapy  
\*Carcinoma, Transitional Cell: DT, drug therapy  
Suramin: AD, administration & dosage  
\*Suramin: TU, therapeutic use  
Treatment Outcome

CAS REGISTRY NO.: 145-63-1 (Suramin)  
CHEMICAL NAME: 0 (Antineoplastic Agents)

L122 ANSWER 26 OF 28 MEDLINE on STN DUPLICATE 7  
ACCESSION NUMBER: 91003939 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 2208069  
TITLE: The concentration of glucose in the culture medium  
determines the effect of suramin on the growth and  
differentiation of the human colonic  
adenocarcinoma cell clone HT29-D4.  
AUTHOR: Rabenandrasana C; Baghdiguian S; Roccabianca M; Brunet M;  
Marvaldi J; Fantini J  
CORPORATE SOURCE: CNRS URA 202, Université de Provence, Marseille, France.  
SOURCE: Cancer letters, (1990 Sep) 53 (2-3) 109-15.  
Journal code: 7600053. ISSN: 0304-3835.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199011  
ENTRY DATE: Entered STN: 19910117  
Last Updated on STN: 19970203  
Entered Medline: 19901115

## ABSTRACT:

Suramin, a drug currently used for advanced malignancy, induces the differentiation of the human colonic adenocarcinoma cell clone HT29-D4 and this process is correlated with a decreased glycolytic activity. We investigated the effects of suramin on HT29-D4 cells in the presence of various glucose concentrations. The main result of this study is that suramin has only an effect on HT29-D4 cell growth and differentiation when the concentration of glucose is above 10 mM. Therefore the efficiency of suramin as an anticancer drug may be greater on poorly differentiated tumoral cells with a high proliferative capacity.

CONTROLLED TERM: Check Tags: Human; In Vitro; Support, Non-U.S. Gov't.

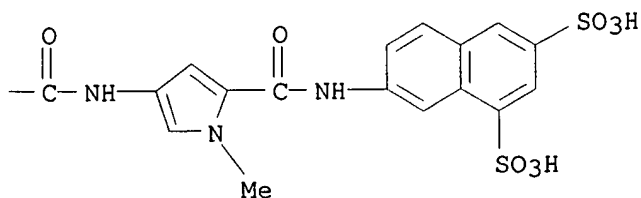
\*Adenocarcinoma: DT, drug therapy  
Adenocarcinoma: ME, metabolism  
\*Colonic Neoplasms: DT, drug therapy  
Colonic Neoplasms: ME, metabolism  
Culture Media  
Glucose: ME, metabolism  
\*Glucose: PD, pharmacology  
Microscopy, Electron  
\*Suramin: TU, therapeutic use  
\*Tumor Cells, Cultured: DE, drug effects  
Tumor Cells, Cultured: ME, metabolism

CAS REGISTRY NO.: 145-63-1 (Suramin); 50-99-7 (Glucose)  
CHEMICAL NAME: 0 (Culture Media)

L122 ANSWER 27 OF 28 MEDLINE on STN DUPLICATE 8  
ACCESSION NUMBER: 89170311 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 2924693  
TITLE: [Treatment of metastatic adrenal carcinoma with suramin].  
Behandlung des metastasierten Nebennierenkarzinoms mit  
Suramin.  
AUTHOR: Allolio B; Jaursch-Hancke C; Reincke M; Arlt W; Metzler U;  
Winkelmann W  
CORPORATE SOURCE: Medizinische Universitätsklinik II und Poliklinik, Köln.

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PAGE 1-B



24 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

24 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L123 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN

RN 145-63-1 REGISTRY

CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[carbonylbis(imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino)]bis- (9CI)  
(CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1,3,5-Naphthalenetrisulfonic acid, 8,8'-[ureylenebis(m-phenylenecarbonylimino(4-methyl-m-phenylene)carbonylimino)]di- (8CI)

OTHER NAMES:

CN 8,8'-[Ureylenebis(m-phenylenecarbonylimino(4-methyl-m-phenylene)carbonylimino)]di-1,3,5-naphthalenetrisulfonic acid

CN Farma

CN Farma 939

CN Fourneau

CN Naganol

CN Suramin

CN Suramine

MF C51 H40 N6 O23 S6

CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CBNB, CHEMCATS, CHEMLIST, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSRESEARCH, IPA, MEDLINE, NAPRALERT, NIOSHTIC, PHAR, PROMT, RTECS\*, SYNTHLINE, TOXCENTER, TULSA, USAN, USPAT2, USPATFULL, VETU

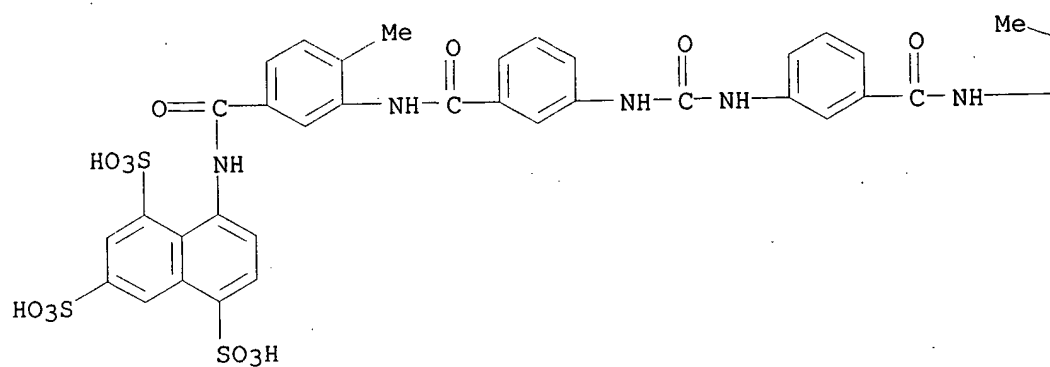
(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*

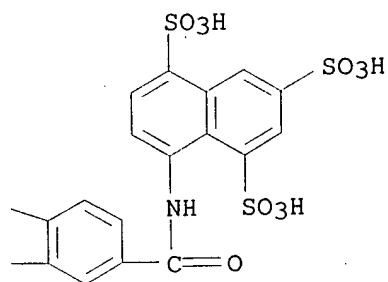
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

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PAGE 1-A



PAGE 1-B



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1329 REFERENCES IN FILE CA (1907 TO DATE)  
37 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
1332 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 8 MAR 2004 HIGHEST RN 660388-34-1  
DICTIONARY FILE UPDATES: 8 MAR 2004 HIGHEST RN 660388-34-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> s 145-63-1 or 154788-16-6

1 145-63-1  
(145-63-1/RN)  
1 154788-16-6  
(154788-16-6/RN)  
L123 2 145-63-1 OR 154788-16-6

*Medline / Cancerlit hit Registry #'s*

=> d ide 1-

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L123 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN

RN 154788-16-6 REGISTRY

CN 1,3-Naphthalenedisulfonic acid, 7,7'-[carbonylbis[imino(1-methyl-1H-pyrrole-4,2-diyl)carbonylimino(1-methyl-1H-pyrrole-4,2-diyl)carbonylimino]]bis-, tetrasodium salt (9CI) (CA INDEX NAME)

OTHER NAMES:

CN FCE 26644

CN PNU 145156E

CN PNU 151484

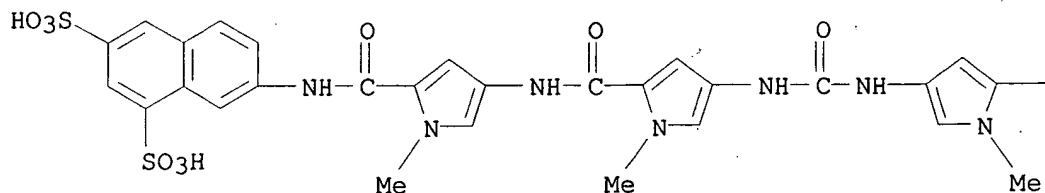
MF C45 H40 N10 O17 S4 . 4 Na

SR CA

LC STN Files: ADISINSIGHT, BIOSIS, CA, CANCERLIT, CAPLUS, IMSDRUGNEWS, IMSRESEARCH, MEDLINE, PHAR, PROMT, TOXCENTER, USPATFULL

CRN (159537-58-3)

PAGE 1-A



● 4 Na

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**\*Neoplasms: DT, drug therapy**

Patient Selection

CAS REGISTRY NO.: 154788-16-6 (FCE 26644) - Registry record printed at the end of this section  
CHEMICAL NAME: 0 (Angiogenesis Inhibitors); 0 (Distamycins)

L122 ANSWER 21 OF 28 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 2000302179 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10845556  
TITLE: Antiangiogenic, antitumoural and antimetastatic effects of two distamycin A derivatives with anti-HIV-1 Tat activity in a Kaposi's sarcoma-like murine model.  
AUTHOR: Rossati L; Campioni D; Sola F; Leone L; Ferrante L; TrabANELLI C; Ciomei M; Montesi M; Rocchetti R; Talevi S; Bompadre S; Caputo A; Barbanti-Brodano G; Corallini A  
CORPORATE SOURCE: Institute of Biomedical Sciences, University of Ancona, Italy.. possati@popcsi.unian.it  
SOURCE: Clinical & experimental metastasis, (1999) 17 (7) 575-82. Journal code: 8409970. ISSN: 0262-0898.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; AIDS  
ENTRY MONTH: 200006  
ENTRY DATE: Entered STN: 20000706  
Last Updated on STN: 20000706  
Entered Medline: 20000627

**ABSTRACT:**

The antiangiogenic, antitumoural and antimetastatic effects of two novel sulphonic derivatives of distamycin A, PNU145156E and PNU153429, were studied in a Kaposi's sarcoma-like tumour model obtained by injecting nude mice with cells releasing extracellular HIV-Tat protein, derived from a tumour which developed in a BK virus/tat transgenic mouse. Both PNU145156E and PNU153429 were administered intraperitoneally every fourth day for three weeks at doses of 100 or 50 mg/kg of body weight respectively, starting one day after injecting the tumour cells. Both drugs delayed tumour growth in nude mice, preventing neovascularization induced by the Tat protein. PNU153429 also significantly reduced the number and size of spontaneous tumour metastases. Both effects on tumour growth and metastases were augmented by treating simultaneously nude mice with 7.5 mg/kg of body weight of minocycline given per os daily for four weeks starting four days after injecting the tumour cells. Neither acute nor chronic toxic side-effects were observed during the life span of treated nude mice. Due to their antiangiogenic and anti-Tat effects, these drugs are promising for the treatment of Kaposi's sarcoma in AIDS patients.

CONTROLLED TERM: Check Tags: Female; Male; Support, Non-U.S. Gov't  
Angiogenesis Inhibitors: PD, pharmacology  
\*Angiogenesis Inhibitors: TU, therapeutic use  
Angiogenesis Inhibitors: TO, toxicity  
Animals  
Antineoplastic Agents: PD, pharmacology  
\*Antineoplastic Agents: TU, therapeutic use  
Antineoplastic Agents: TO, toxicity  
Antineoplastic Combined Chemotherapy Protocols: TU, therapeutic use  
Distamycins: AD, administration & dosage  
Distamycins: PD, pharmacology  
\*Distamycins: TU, therapeutic use  
Distamycins: TO, toxicity  
Drug Screening Assays, Antitumor  
\*Gene Products, tat: AI, antagonists & inhibitors  
Genes, tat  
\*HIV-1: GE, genetics  
Mice  
Mice, Nude

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Mice, Transgenic  
Minocycline: AD, administration & dosage  
\*Neoplasm Metastasis: DT, drug therapy  
\*Neoplasm Proteins: AI, antagonists & inhibitors  
Neoplasm Transplantation  
\*Neovascularization, Pathologic: DT, drug therapy  
\*Sarcoma, Kaposi: DT, drug therapy  
Sarcoma, Kaposi: ET, etiology  
Sarcoma, Kaposi: PA, pathology  
Transfection  
CAS REGISTRY NO.: 10118-90-8 (Minocycline); 154788-16-6 (FCE 26644)  
CHEMICAL NAME: 0 (Angiogenesis Inhibitors); 0 (Antineoplastic Agents); 0  
(Antineoplastic Combined Chemotherapy Protocols); 0  
(Distamycins); 0 (Gene Products, tat); 0 (Neoplasm  
Proteins); 0 (PNU 153429)

L122 ANSWER 22 OF 28 MEDLINE on STN DUPLICATE 3  
ACCESSION NUMBER: 1999380181 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10449994  
TITLE: Effects of suramin on anastomotic colon tumors in  
a rat model.  
AUTHOR: Lauwers P; Hubens G; Hendriks J; Vermeulen P; Schuerwegh A;  
Stevens W J; De Clerck L S; Dirix L; Van Marck E; Hubens A;  
Eyskens E  
CORPORATE SOURCE: Laboratory for Experimental Surgery and Department of  
Immunology, 'Medisch Instituut Sint Augustinus', Antwerp,  
Belgium.  
SOURCE: European surgical research. Europaische chirurgische  
Forschung. Recherches chirurgicales europeennes, (1999) 31  
(4) 347-56.  
Journal code: 0174752. ISSN: 0014-312X.  
PUB. COUNTRY: Switzerland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199910  
ENTRY DATE: Entered STN: 19991101  
Last Updated on STN: 19991101  
Entered Medline: 19991021

## ABSTRACT:

BACKGROUND: The development of antiangiogenic drugs offers new promise in the treatment of malignancy. Suramin has been reported to inhibit tumor growth by blocking angiogenesis and has been used in clinical trials. The aim of the present study was to examine the effects of suramin on colonic anastomotic tumors in the rat. METHODS: (a) Colonic anastomotic tumor was induced in 120 WAG/RIJ rats. Half of the animals were given 100 mg/kg of suramin intraperitoneally at the time of tumor induction. Rats were sacrificed after 2, 4 and 8 weeks; tumor take and tumor weight were evaluated. (b) The number of red blood cell clusters per x 400 field was counted in each tumor. (c) A lymphocyte transformation test was performed in four groups of animals, 2 weeks before and 2 weeks after tumor implantation and/or suramin administration. RESULTS: (a) A significant enhancement of tumor growth was observed in the suramin-treated animals. (b) This was accompanied by a significant increase in functional blood vessels. (c) Suramin-treated rats had markedly decreased lymphocyte stimulation, pointing to a possible immunosuppressive effect. CONCLUSIONS: The growth of an anastomotic \*\*\*colon\*\*\* tumor is rather enhanced by a single intraperitoneal administration of 100 mg/kg suramin in the rat, possibly by an unexpected immunosuppressive effect.

CONTROLLED TERM: Check Tags: Comparative Study; Male  
Adenocarcinoma: BS, blood supply  
\*Adenocarcinoma: DT, drug therapy  
Adenocarcinoma: IM, immunology

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